

# **"A PROSPECTIVE STUDY OF SOLITARY NODULE THYROID"**

**Dissertation submitted to**

**THE TAMILNADU Dr.M.G.R MEDICAL UNIVERSITY**

**In partial fulfilment of the degree of**

**M.S. GENERAL SURGERY**

**Branch - 1**



**PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH**

**DEPARTMENT OF GENERAL SURGERY**

**APRIL – 2015**

## **CERTIFICATE**

This is to certify that this dissertation entitled “**A PROSPECTIVE STUDY OF SOLITARY NODULE THYROID**” is a record of bonafide research work done by Dr.B.Meenalosani, under my guidance and supervision in the Department of General Surgery, PSG Institute of Medical Sciences and Research, Coimbatore – 641004.

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February 11, 2014

To  
Dr B Meenalosani  
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The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on January 22, 2014 in its expedited review meeting held at IHEC Secretariat, PSG IMS&R, between 10.00 am and 11.00 am, and discussed your study proposal entitled:

*"A prospective study of Solitary Nodule Thyroid"*

The following documents were received for review:

1. Duly filled application form
2. Proposal
3. Informed Consent Forms (Ver 1.1)
4. Data collection tool
5. CV
6. Budget

After due consideration, the Committee has decided to approve the study.

The members who attended the meeting at which your study proposal was discussed are as follows:

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Dr S Bhuvaneshwari	M.D	Clinical Pharmacologist Member - Secretary	Female	Yes	Yes
Dr Sudha Ramalingam	M.D	Epidemiologist Alt. Member - Secretary	Female	Yes	Yes
Dr Y S Sivan	Ph D	Member - Social Scientist	Male	Yes	Yes
Dr D Vijaya	Ph D	Member - Basic Scientist	Female	Yes	Yes

The approval is valid for one year.

We request you to intimate the date of initiation of the study to IHEC, PSG IMS&R and also, after completion of the project, please submit completion report to IHEC.



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This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

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Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

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### INTRODUCTION

Thyroid diseases are common worldwide, affecting 3-5% of the population. They include hypothyroidism, enlargement of the gland both diffuse and nodular, solitary nodules both benign and malignant, and inflammatory diseases.

Goitre means an enlargement of the thyroid gland that is at least twice its normal size. The adult thyroid gland weighs between 20 and 30 grams. It is usually non palpable or barely palpable. Solitary nodule is a single or discrete nodule confined to one lobe of the thyroid and the opposite lobe may not be visible or palpable (True solitary nodule) about 70%. STN presents in 1-3% of the adult population and is common in women. The incidence of malignancy is 12-15% and more chance of malignancy is in a cold and solid nodule. More than 25% STN in men is more likely malignant. In patients younger than 25 or older than 60 the malignancy rate for thyroid nodule as high as 60% has been described. Many nodules that appear solitary upon examination are found to be a part of a multi nodular goitre (dominant) at surgical or histological examination (30%). The risk of carcinoma in a dominant nodule in multi nodular gland is approximately 5%.

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## **DECLARATION**

I, Dr.B.Meenalosani, solemnly declare that this dissertation “**A PROSPECTIVE STUDY OF SOLITARY NODULE THYROID**” is a bonafide record of work done by me in the Department of General Surgery, PSG institute of Medical Sciences & Research, Coimbatore, under the guidance of Dr.S. Prem Kumar, Professor & HOD of Surgery. This dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfilment of the University regulations for the award of MS Degree (General Surgery) Branch-I, Examination to be held in April 2015.

Place: Coimbatore

Date: 30th September, 2014

**(DR.B.MEENALOSANI)**

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## INTRODUCTION

Thyroid diseases are common worldwide, affecting 3-5% of the population.<sup>1</sup> They include enlargement of the gland both diffuse and nodular, solitary nodule both benign and malignant, and inflammatory diseases.

Goiter means an enlargement of the thyroid gland that is at least twice its normal size. The adult thyroid gland weighs between 20 and 30 grams. It is usually non palpable or barely palpable. Solitary nodule is a single or discrete nodule confined to one lobe of the thyroid and the opposite lobe may not be visible or palpable (True solitary nodule) about 70%. Solitary nodule thyroid (SNT) presents in 1-3% of the adult population and is common in women. The incidence of malignancy is 12-15% and more chance of malignancy is in a cold and solid nodule. More than 25% SNT in men is more likely malignant. In patients younger than 25 or older than 60, the malignancy rate for thyroid nodule as high as 60% has been described. Many nodules that appear solitary upon examination are found to be a part of a multi nodular goitre (dominant) at surgical or histological examination (30%). The risk of carcinoma in a dominant nodule in multi nodular gland is approximately 5%.<sup>2</sup>

A dominant nodule in multi nodular gland is considered benign unless some findings are suggestive of malignancy, like laryngeal nerve

palsy or enlarged lymph nodes, whereas a STN is considered malignant until proved benign, especially in young patients.

## **AIM OF THE STUDY**

- To know mode of presentation of solitary nodule thyroid
- To know incidence of malignancy
- To know the role of FNAC in solitary nodule thyroid

## **REVIEW OF LITERATURE**

### **HISTORICAL BACKGROUND**

Goiter (from the Latin word *guttur*, throat), defined as an enlargement of the thyroid, has been recognized since 2700 B.C. In 1619, Hieronymus Fabricius ab Aquapendente recognized that goiters arose from thyroid gland.

Thyroid surgery has been performed since ancient times.

In the first and second centuries, Celsus and Galen described cervical masses such as cysts, tuberculous lymph nodes (scrofula), and goiters. Celsus reported that the operation for removal of such a mass was dangerous.<sup>3</sup> In communities where goitre was endemic, it was considered an inoperable and frequently fatal affliction as death was commonly the result of respiratory obstruction. Surgical relief was invoked for disfigurement, dyspnoea or dysphagia.<sup>4</sup> Albucasin, the 11th century surgeon of Corodoba (Spain) also explained extirpation of the gland.<sup>5</sup>

The first documented partial thyroidectomy was carried out by Pierre Joseph Desault in 1791. He removed a mass from thyroid through a vertical incision, tying off, superior/inferior thyroid arteries and then dissecting the gland from trachea.

The leading thyroid surgeons at the second half of the nineteenth century were Theodor Kocher (1841-1917) of Berne, a scholarly and meticulous surgeon, and Theodor Billroth (1829-1894) of Vienna, a great extrovert and fast operator. Both European Surgeons performed thousands of thyroidectomies, with progressively better results.<sup>6</sup>

Theodore Kocher was the Professor of Surgery in Switzerland. He practiced gentle meticulous surgery which spared even parathyroid glands which were not yet discovered and he anatomically appreciated the recurrent laryngeal nerve. Using such principles, the mortality of thyroid surgery reduced from almost 59% to approximately 0.2%. A more important discovery by Kocher was that after total thyroidectomy, myxoedema could develop and he demonstrated that this complication can be avoided by doing a subtotal thyroidectomy. In 1909, For his work in medical understanding of the thyroid diseases, Kocher was awarded the Nobel Prize. THEODOR KOCHER IS REGARDED AS FATHER OF THYROID SURGERY.

He reported 146 thyroidectomies from 1850 to 1877 with mortality being 21%. He also reported 600 cases performed with 0.5% mortality in 1898 which revolutionized the technique and method of thyroid Surgery and earned him Nobel Prize for medicine in 1909.<sup>3</sup>



**Fig. 1: Theodor Kocher (1841-1917)**

From the words of Kocher : "There are three types of operations for thyroid disease: (i) Total extirpation, (ii) Partial thyroidectomy or resection, (iii) Enucleation.<sup>7,8</sup> He recognized pressure of the goitre as the cause of softening of the cartilages, distortion of the trachea and the consequent respiratory embarrassment.<sup>7,8</sup>

The indications of operation were extended to include the prevention of complications, especially in patients with thyrotoxicosis and thyroid cancer. Following the development of non-surgical measures to manage most cases of hyperthyroidism and colloid goitre, due to

availability of radioactive iodine, anti thyroid drugs and iodination of salt, surgical attention was directed to nodules, both benign and malignant but with emphasis on the latter.

## **PARATHYROID GLANDS:**

The first description of the parathyroid glands was by the London anatomist and curator of the Natural History Museum, Sir Richard Owen, in 1850. The respective paper was eventually published in the Zoological Proceedings of London <sup>9</sup>. He was not given credit for his observation because he never performed histological confirmation. This state of affairs lasted until 1887 when the medical student Ivar Sandström described tiny glandular elements in 50 dissected human bodies. He gave a comprehensive description of their appearance, position, size, and blood supply and named them "glandulae parathyreoideae."

The early operations were accompanied by a frightful mortality i.e 41% in 1850. Recent statistics show a fraction of 1%. The dangers of the earlier operations were haemorrhage, thrombosis of the jugular and subclavian veins, air emboli, injuries to the recurrent laryngeal and vagus nerves, damage to the trachea or esophagus. The sequelae were mediastinitis with or without abscess formation, phlegmon and fistula of the neck, erysipelas, pyrexemia, tetanus, inflammation of the lung and pleura, tetany and cachexia strumipriva. Death was due to haemorrhage,



either primary or secondary, or to the then almost inevitable sepsis.<sup>10</sup> Anton Wolfler first called attention to the danger of injuring the recurrent nerve when ligating the inferior thyroid artery.<sup>11</sup>

## **HISTORY OF THYROID ULTRASOUND <sup>12</sup>**

Thyroid gland is suitable for ultrasound study because it is superficial, vascular, and due to its size and echogenicity. Also, thyroid has a high incidence of nodularity, most of which are benign. Many of the structural abnormalities of thyroid require evaluation and monitoring, but do not need intervention. So, thyroid was one of the first organs which was studied well by the ultrasound. Thyroid ultrasound reports first appeared in late 1960s. Ultrasound of thyroid underwent a dramatic transformation from cryptic deflections on oscilloscope which was produced by A-mode scanning, proceeding to barely recognized B-mode images, and then the initial low resolution gray scale, followed by the modern high resolution image. Recent advances made in technology include the harmonic imaging, then contrast studies, and the three-dimensional reconstruction.

Pierre and Jacques Curie, in 1880, discovered piezoelectric effect, and determined that electric current which is applied across a crystal will result in vibration that will generate sound waves, and the sound waves will, in turn, produce electric voltage. Piezoelectric transducers were able

to produce sonic waves in audible range and the ultrasonic waves above human hearing range.

In 1912, first operating sonar system was produced after two years of the sinking of Titanic. The system was able to detect an iceberg situated two miles away from the ship. The system was capable of detecting, and not localizing, objects within sonar range. In the next 30 years sonar navigation improved.

In 1940s, ultrasound's first medical application occurred. They observed that high intensity sound waves were able to damage the tissues, so the lower intensities were used for therapeutic purposes. The focused sound waves were utilised to heat the tissues mildly for treatment of rheumatoid arthritis, and to destroy basal ganglia for treatment of Parkinson's disease.

In 1942, ultrasound was first applied for diagnostic purposes. In the paper titled "Hyperphonagraphy of Brain", cerebral ventricles were localized by Karl Theodore Dussic using ultrasound. He relied on sound waves transmission.

In the early 1950's, first imaging by the reflection of pulse-echo was attempted. A-mode scanning provided information in a single dimension. This was used for detecting brain tumors, midline shifts,

localizing foreign bodies in eye, and detecting detached retinas. With the first idea that the ultrasound might help in cancer detecting, John Julian Wild observed that gastric carcinomas could be more echogenic compared to normal gastric tissues. He also studied the breast nodules, and was able to detect their size with 90% accuracy.

In the late 1950's 2D B-mode scanners were first developed. High resolution B-mode ultrasound is an inexpensive and rapid method of examining the neck and is used to assess palpable abnormalities and guide biopsies.<sup>13</sup> In the neck, ultrasound was initially used as a Doppler to study carotid vessels. It was then found that ultrasound could also be used to detect soft tissues and thyroid was one of first soft tissue organs identified by the ultrasound.

Optimal examination of the structures of the neck requires high resolution (between 5-20MHz) transducers. The use of higher frequency improves spatial resolution, allowing nearly microscopic resolution of very small areas, but has very limited depth penetration.

A limitation of ultrasound is that it is operator dependant and the deep structures cannot be identified. Ultrasound guided fine needle cytology allows the accurate and rapid diagnosis of neck masses.<sup>14</sup>

## **HISTORY OF FINE NEEDLE ASPIRATION CYTOLOGY <sup>15</sup>**

First reports of fine-needle aspiration cytology (FNAC) as a technique for obtaining diagnostic material date back to the 19<sup>th</sup> century when, at London, aspiration was undertaken on a large mass in the liver by the Surgeons Stanley and Earle. Sir James Paget advocated the use of aspiration as an investigative technique in his lectures. Menetrier was probably the first to use aspiration to investigate lung cancer. Some years later, at the beginning of the 20<sup>th</sup> century, Griegg and Gray published the results of a lymph node aspirate for trypanosomiasis. The first large scale study was carried out at the Memorial Hospital, New York, by the pioneering team of Martin, Ellis and Stewart, who used a thicker caliber needle (18-gauge), than the needles commonly in use today.

True fine needles for aspiration (22- to 27-gauge) were first introduced in Europe in the 1950s by Lopez-Cardozo in the Netherlands and Soderstrom in Sweden. It was however, Zajiecek, in Stockholm, who determined diagnostic accuracy in a variety of conditions. At that time, the European clinicians developed the Romanowky and May-Grunwald Giemsa stains for use in air-dried smears to allow for rapid interpretation. Despite their success, it was not until the 1980s that FNAC became widely used.

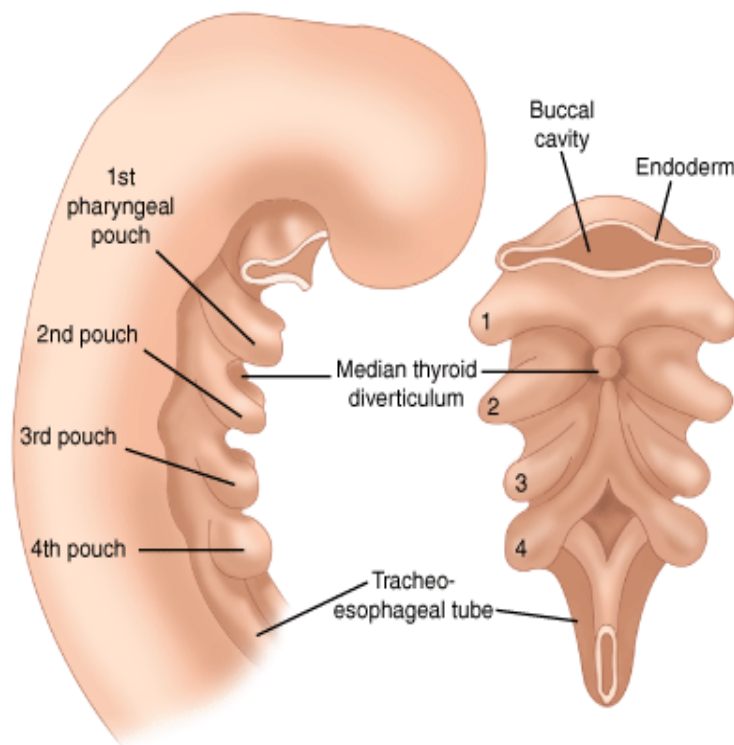
## **FNAC as a tool in clinical investigation**

FNAC was initially conceived as a means to confirm a clinical suspicion of local recurrence or metastasis of known cancer without subjecting the patient to further surgical intervention. Following the success in this area, the interest focused on preliminary preoperative diagnosis of all kinds of neoplastic processes, benign or malignant, in any organ or tissue of the body and on definitive, specific diagnosis inoperable cases as guide to rational treatment.

With the development of techniques such as FNAC and ultrasound, the performance of thyroidectomy has become selective, unlike in the past when surgery was recommended for nearly all Multinodular goitres.

## EMBRYOLOGY<sup>16</sup>

The primordial thyroid gland is first identifiable during the fourth week of gestation, beginning as an endodermal invagination of the tongue at the site of the foramen cecum.



**Fig. 2: Embryology of Thyroid**

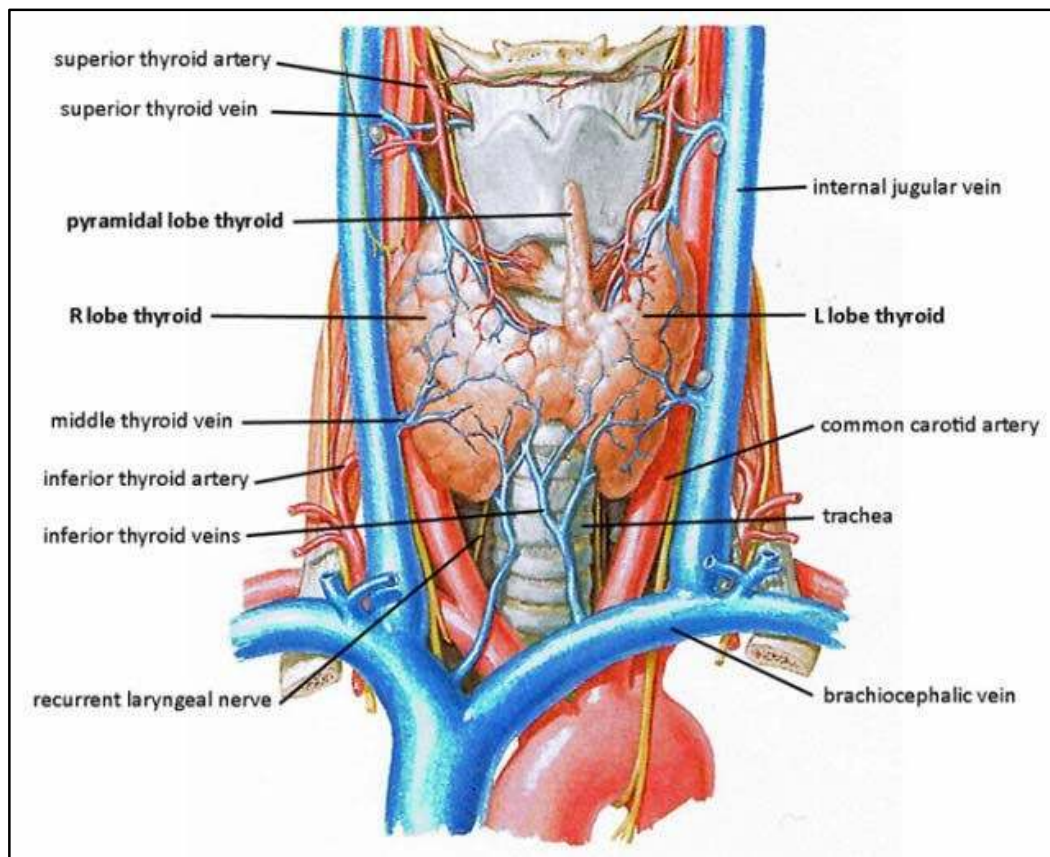
Thyroid gland mainly develops from the thyroglossal duct. Parafoollicular cells are derived from the caudal pharyngeal complex (derived from 4th and 5th pharyngeal pouches) separate by midline swelling called the tuberculum impar. Immediately behind the tuberculum, the epithelium of the floor of the pharynx shows a thickening

in the midline. This region is soon depressed below the surface to form a diverticulum called the thyroglossal duct. During 6<sup>th</sup> week of embryonic life, the diverticular thyroid structure becomes bilobar and descends to its ultimate position with a lobe on either side of trachea in the neck, later these lobes are connected by isthmus. At the same time, normally the thyroglossal duct disappears.

The distal part of the thyroglossal duct degenerates but may remain as a pyramidal lobe <sup>17</sup>. There is also a contribution to the thyroid from the fifth pharyngeal pouch (ultimobranchial body). These cells are believed to be neural crest in origin. They migrate into the thyroid and differentiate into the calcitonin-producing C cells.

By 8th week of embryonic development, small cavities appear in the thyroid tissue. They expand and proliferate, as colloid appears in follicles. Formation of follicles is completed by fifth month of fetal life, thereafter the new follicles are formed by budding and division of existing follicles.

Thyroid is the earliest glandular structure to appear. It becomes functional during the third month of development of fetus. <sup>17</sup>



**Figure 3:Adult thyroid gland**

### **SURGICALANATOMY<sup>18,19,20,21,22</sup>**

A normally developed adult thyroid is a bilobed structure that lies next to the thyroid cartilage in a position anterior and lateral to the junction of the larynx and trachea. In this position, the thyroid encircles about 75% of the diameter of the junction of the larynx and the upper part of the trachea.

Thyroid gland averagely weighs 20-25 Gms. It is larger in females than in males and increases further during pregnancy and menstruation.



Thyroid gland has two lobes, which are shaped like slender pears, holding onto anterolateral aspect of trachea from level of thyroid cartilage to 5th or the 6th tracheal rings. Right lobe is usually larger compared to left and the two lobes join together across midline by an isthmus which is quite firmly attached to anterior surface of trachea, at level of 2nd and the 3rd tracheal ring. A small sized pyramidal lobe usually arises from isthmus along the upper border close to midline. Thyroid gland is enclosed by the fascia and strap muscles and laterally, it is located under anterior borders of sternocleidomastoid muscles.

A thin layer of connective tissue surrounds the thyroid. This tissue is part of the fascial layer that invests the trachea. This fascia coalesces with the thyroid capsule posteriorly and laterally to form a suspensory ligament known as the ligament of Berry. The ligament of Berry is closely attached to the cricoid cartilage and has important surgical implications because of its relationship to the recurrent laryngeal nerve.

The superficial surface of the gland is covered by the infrahyoid and sternomastoid muscles with its fascial coverings.

The medial surface related to the trachea and esophagus, two nerves recurrent and external laryngeal nerves, two muscles inferior constrictor and cricothyroid.

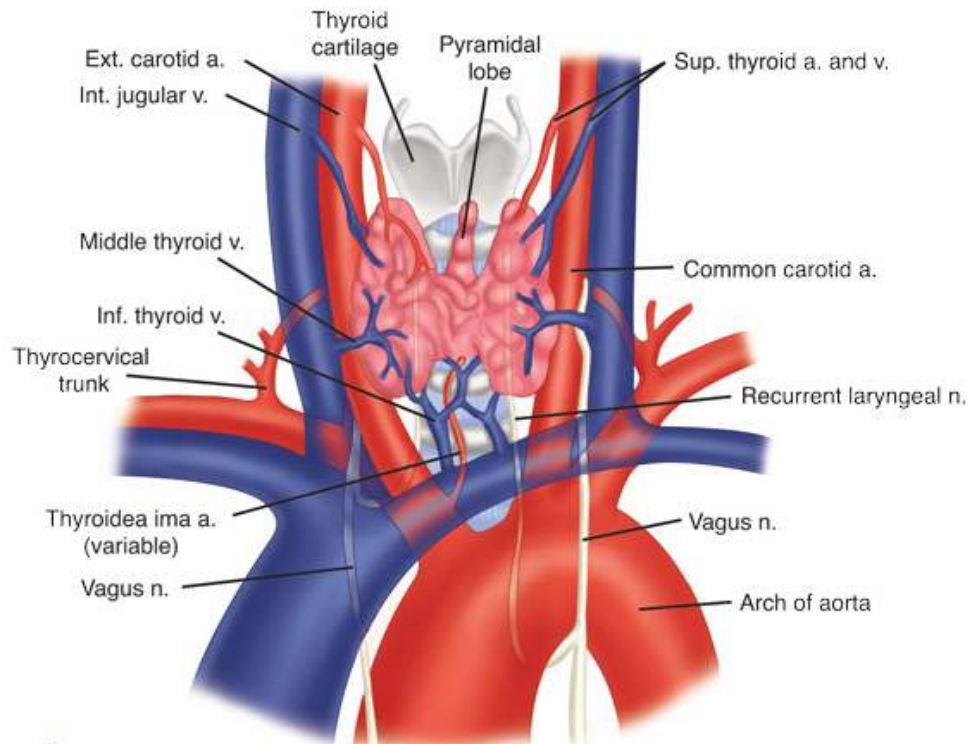
The posterior surface overlaps the common carotid artery and covers the terminal part of inferior thyroid artery.

Because of its fascial attachments the gland moves upwards with swallowing and therefore slides under the examining fingers. The normal gland can be felt in thin necks. It is soft and supple and the tracheal rings can be palpated through it.

**The important anatomical features with surgical relevance are:**

**THE MUSCULO FASCIAL COVERINGS:** The strap muscles are ensheathed by the general investing layer of cervical fascia and this unites them in the midline. These muscles are applied to the anterior surface of the gland, but separated from it by a loose condensation of fascia derived from the pretracheal fascia. This false capsule covers the gland which is enclosed by its diaphanous true capsule with its very rich blood supply, clearly visible just beneath its surface. The nerve supply of these muscles, the sternohyoid and its deeper neighbour, the sternothyroid comes from cervical roots 1, 2 and 3 via branches from the ansa cervicalis. These branches enter the muscles at its lateral border and on the deep surface and though it is not often necessary, the muscles may be divided transversely to facilitate access to the gland provided they are re-sutured, there does not appear to be any impairment of function.

## BLOOD SUPPLY:



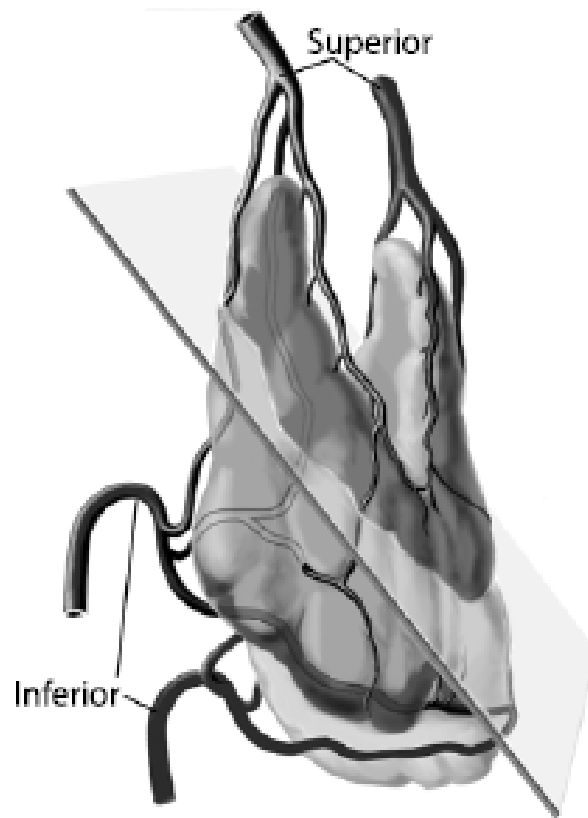
**Fig . 4**

The arterial supply to the thyroid gland consists of four main arteries, two superior and two inferior.

**( a ) Superior thyroid artery:** The superior thyroid artery is the first branch of the external carotid artery and arises immediately above the bifurcation of the common carotid artery. The superior thyroid artery courses medially onto the surface of the inferior pharyngeal constrictor muscle and enters the apex of the superior pole. As the superior thyroid artery proceeds medially, it is adjacent to the external branch of the superior laryngeal nerve, and thus care must be taken to not damage it when controlling the artery.

**( b ) Inferior thyroid artery:** It is a branch of thyrocervical trunk which arises from the first part of the subclavian artery. In the neck, it passes behind the carotid artery. Before entering the pretracheal fascia, it divides into 4 or 5 branches that pierce the fascia separately to reach the lower pole of the gland. The inferior thyroid artery gives off oesophageal and tracheal branches before its terminal distribution into the gland. Inferior thyroid artery may be absent congenitally in 35% of the patients. The inferior thyroid artery supplies the lower 2/3rd of the lobe and the lower ½ of isthmus with parotid glands. This makes a major share in thyroid blood supply.

The inferior thyroid artery has important anatomic relationships. The recurrent laryngeal nerve is usually directly adjacent (in either an anterior or posterior position) to inferior thyroid artery. So the artery has to be carefully dissected till the nerve is identified. Additionally, this artery usually supplies both parathyroid glands, so parathyroids should be evaluated after the artery is ligated.



**Fig. 5: Arterial supply of thyroid and parathyroid glands is divided into a superior and a inferior system.**

**( c ) The Thyroidea Ima Artery:** The thyroidea ima artery from the brachiocephalic trunk extending in front of the trachea is small and surgically irrelevant.

## VEINS

The thyroid gland is drained by following veins.

( a ) **Superior thyroid vein:** It leaves the upper part of the gland, crosses the common carotid artery and terminates into the internal jugular vein or common facial vein.

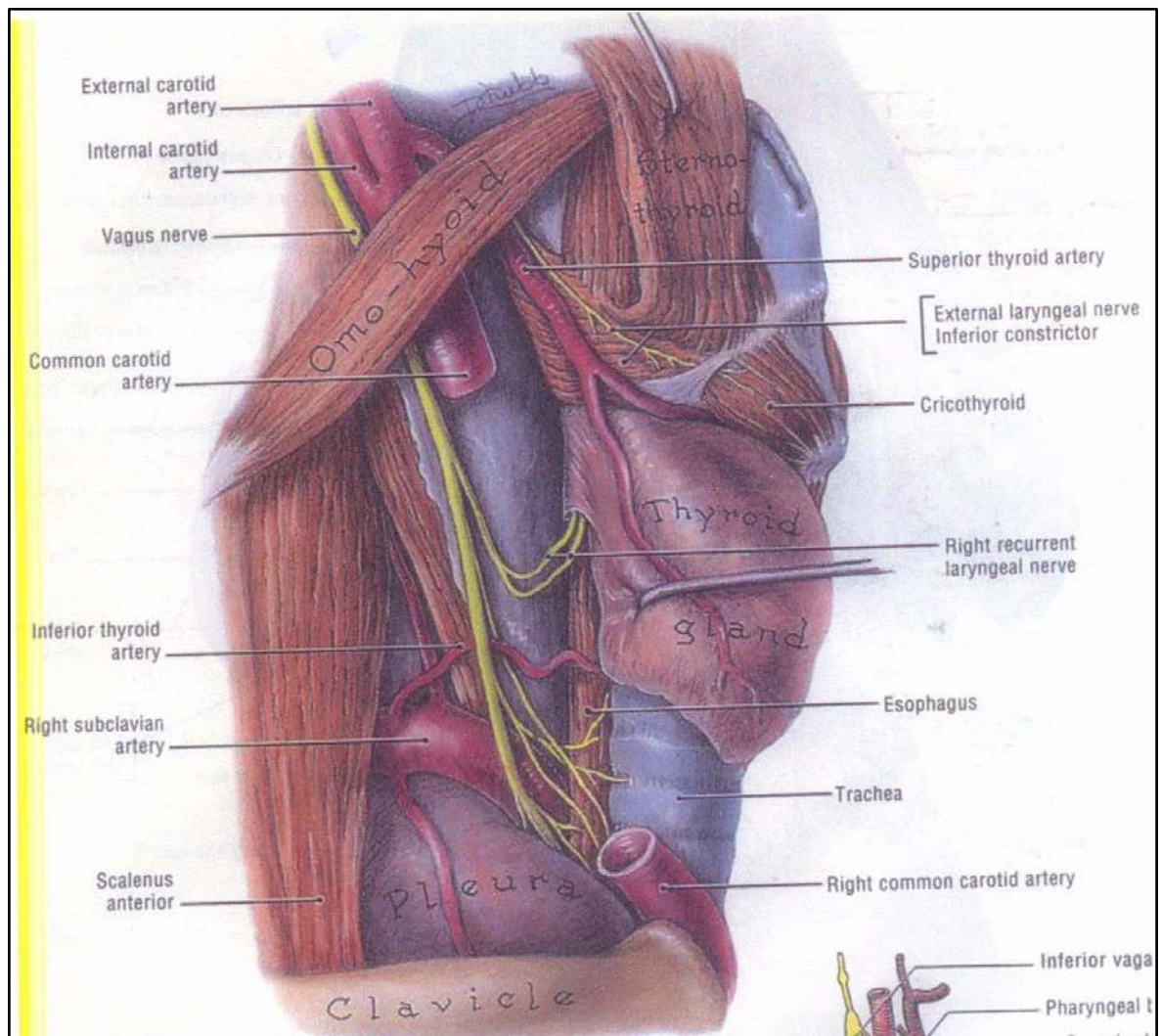
( b ) **Middle thyroid vein:** It leaves the gland at the middle of the lateral part of the lobe, follows the inner border of the omohyoid muscle across the carotid vessels to end in internal jugular vein. It is thick, short and directly enters the jugular vein. It is present only in 30% of individuals.

( c ) **Inferior thyroid vein:** It leaves the Isthmus at the inferior border and runs down in front of the trachea to end in innominate vein of the same side.

( d ) **Fourth thyroid vein:** KOCHER drew attention to the frequent existence of this vein which passes outward between middle and inferior thyroid vein.

**THE IMPORTANT CLOSE SURGICAL RELATIONS OF THE THYROID GLAND:** These are the recurrent laryngeal nerves, the external laryngeal nerves and the parathyroid glands. Like all important relations they should be recognized immediately and cared for respectfully.

***The External Laryngeal Nerve:*** The external laryngeal nerve, a branch of the superior laryngeal nerve, descends on the fascia of the inferior pharyngeal constrictor, relates closely to the superior vascular pedicle of the thyroid and then leaves this at a variable height above the gland to travel medially to its destination in the cricothyroid muscle. It is functionally important for the pitch of the voice, because the cricothyroid muscle is a tensor of the vocal cord. Damage to this nerve alters the voice quite significantly and is especially noticeable in singers.



**Fig. 6: Course of recurrent laryngeal nerve**

The Recurrent laryngeal nerves ascend on either side of the trachea, and each lies just lateral to the ligament of Berry as they enter the larynx. There are a number of important variations. In about 25% of patients the recurrent laryngeal nerve is contained within the ligament as it enters the larynx. On the **right side**, the recurrent laryngeal nerve separates from the vagus as it crosses the subclavian artery; it then passes



posteriorly and ascends in a lateral position to the trachea along the tracheoesophageal groove. The right recurrent laryngeal nerve can usually be found no further than 1 cm lateral to or within the tracheoesophageal groove at the level of the lower border of the thyroid. As it ascends to the midportion of the thyroid, however, the nerve assumes its position within the tracheoesophageal groove. At this location the nerve might divide into one, two, or more branches as it enters the first or second ring of the trachea, with the most important branch disappearing beneath the inferior border of the cricothyroid muscle. The nerve can usually be found immediately anterior or posterior to a main arterial trunk of the inferior thyroid artery at this level. Unusually, a nonrecurrent right laryngeal nerve can arise directly from the vagus and course medially into the larynx. This nonrecurrent anatomy is found in 0.5% to 1.5% of patients. Even more infrequently, patients may have both a recurrent and a nonrecurrent laryngeal nerve on the right. These two nerves usually join in a position beneath the lower border of the thyroid. On the **left side**, the recurrent laryngeal nerve separates from the vagus as that nerve traverses over the arch of the aorta. The left recurrent laryngeal nerve then passes inferior and medial to the aorta and begins to ascend toward the larynx, where it finds its way into the tracheoesophageal groove as it ascends to the level of the lower lobe of the thyroid. Both recurrent laryngeal nerves are consistently found within the

tracheoesophageal groove when they are within 2.5 cm of their entrance into the larynx. These nerves pass either inferior or posterior to an arterial branch of the inferior thyroid artery and eventually enter the larynx at the level of the cricothyroid articulation on the caudal border of the cricothyroid muscle. Here the nerve is immediately adjacent to the superior parathyroid, the inferior thyroid artery, and the most posterior aspect of the thyroid. Great care is needed during surgical dissection in this area because the nerve is essentially tethered as it dives beneath the cricothyroid muscle and can be stretched by overly vigorous dissection.

The nerve usually bifurcates extralaryngeally but often at a point less than 0.5 cm from the cricoid cartilage. Up to 58% of recurrent laryngeal nerves will bifurcate proximal to inferior border of the cricoid cartilage. Extralaryngeal trifurcations exist in approximately 1% of RLNs.

***The parathyroid Glands:*** The number of parathyroids vary from 2 to 6 but in 80 percent of cases there are 4 (2 on each side). The glands are the size of a split pea. They are pink or brown in colour. The superior glands lie on the posterior surface of the middle third of the thyroid, usually above the inferior thyroid artery, but well posterior to this plane. The inferior glands are mostly found on the posterior surface of the lower pole of the thyroid or within 1 cm below the lower pole. They lie in a more

anterior plane than the upper glands. A parathyroid gland is located within the surgical false capsule of the thyroid. Sometimes the parathyroids may be embedded in the thyroid gland. A small parathyroid artery supplies each gland. The lower parathyroid artery comes from the inferior thyroid artery. The upper parathyroid artery arises from the inferior artery or from an anastomosing artery joining the superior and inferior thyroid arteries. They will be at risk during operations on the thyroid gland.

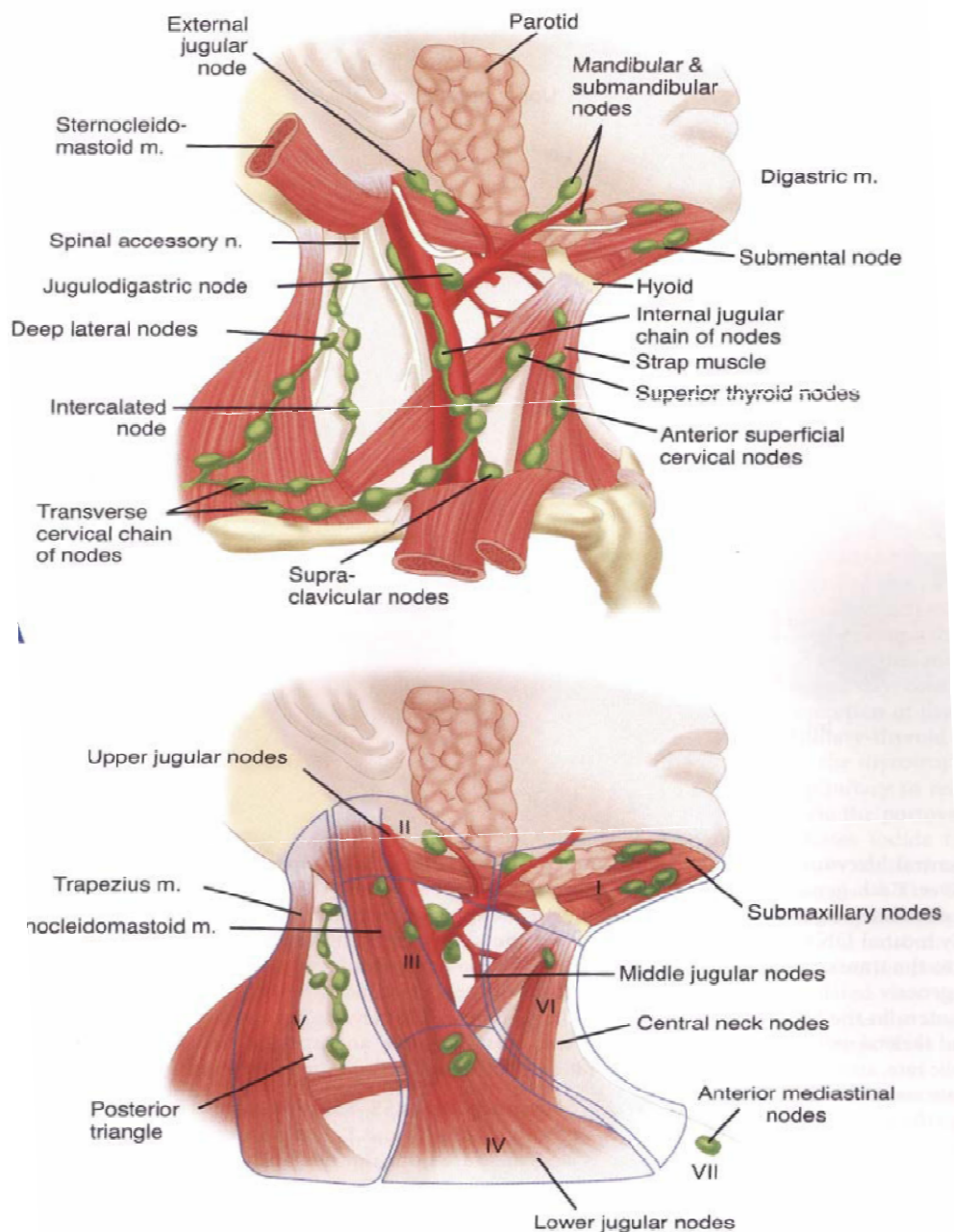
### **LYMPHATICS OF THYROID:**

The gland is drained by two sets of lymphatics

1) ascending and 2) descending each consisting of medial and lateral channels.

#### **Ascending Vessels:**

**Medial:** leave the upper border of the gland and drain into nodes situated on the cricothyroid membrane, the prelaryngeal gland.



**Fig. 7 Lymphatic Drainage**

**Lateral:** leave the upper pole of the gland and run along the superior thyroid artery to the deep cervical nodes situated at the bifurcation of common carotid artery.

**Descending Vessels:**

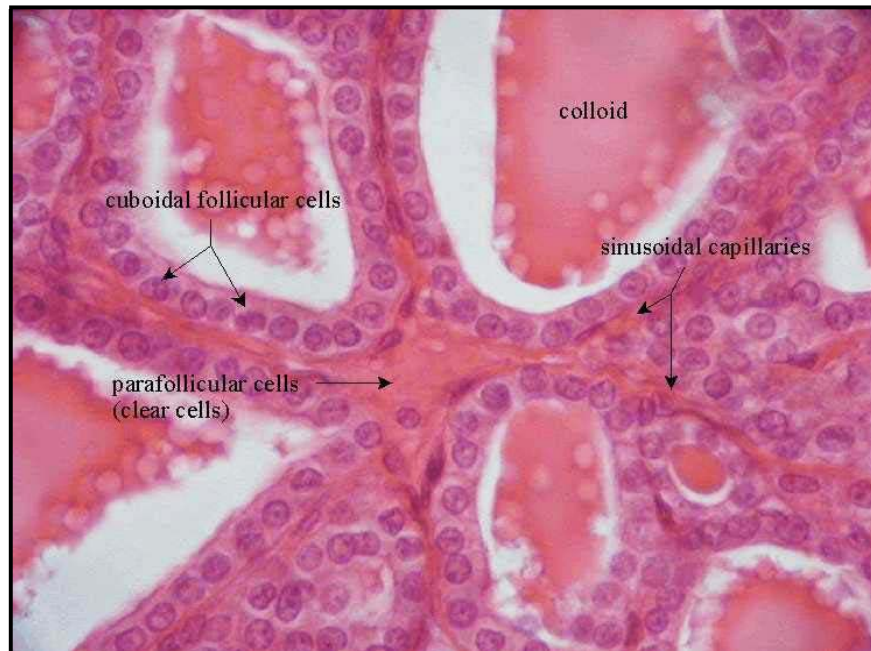
**Medial:** pass to the gland on the trachea, pre-tracheal lymph nodes.

**Lateral:** pass from the deep surface of the gland to small nodes placed on recurrent nerve, the nodes of recurrent chain

The lymph vessels run in the interlobular connective tissue and connect with the network within the capsule of the gland. The ascending lymphatic channels drain the upper border of isthmus and surface of the lobes.

The descending channels drain the major part of isthmus and lower part of lateral lobes. The median lymph node near the isthmus is often involved in thyroid cancer, which is called *Delphian* node

## HISTOLOGY OF THYROID :



**Fig. 8 Histology of thyroid**

The gland is surrounded by a thin connective tissue capsule, which sends in septa dividing the gland into groups of follicles or lobules. There is very little connective tissue between the individual follicles. This connective tissue gives support to the abundant fenestrated capillaries that are present in the gland. <sup>23</sup>

The glandular substance is composed of spherical (acini) follicles with a large lumen. The follicles vary in size and are filled with proteinaceous colloid, which stain acidophilic. <sup>24</sup>

The epithelial cells lining the follicles are cuboidal or columnar according to the activity of the follicle. The average size is about 15  $\mu$ m.

The acini are arranged in subunits of 20 to 40 and demarcated by connective to form lobules, each supplied by an individual artery. The size of the follicles vary, being around 200  $\mu$ m in diameter. <sup>24</sup>

The parafollicular cells or “ C ” cells which stain lighter in colour but are bigger in size are present in the follicular epithelium lying in between the basement membrane and epithelial cells. Some are also present in the interfollicular spaces. <sup>23</sup>

## **PHYSIOLOGY** <sup>25,26</sup>

The thyroid gland maintains the level of metabolism in the tissues that is optimal for their normal function. Thyroid hormones stimulate the consumption of most of the cells in the body, help regulate lipid and carbohydrate metabolism, and are necessary for normal growth and maturation. The thyroid gland is not essential for life, but its absence causes mental and physical slowing, poor resistance to cold, and, in children, mental retardation and dwarfism. Conversely, excess thyroid secretion leads to body wasting, nervousness, tachycardia, tremor, and excess heat production. The thyroid gland also secretes calcitonin, a calcium- lowering hormone.

## **Iodine metabolism**

Iodine is taken in the form of Iodides sea fish; egg and milk are good dietary source of iodide. Dietary iodide is absorbed from upper gastrointestinal tract and carried as inorganic iodide in plasma. Normally thyroid, salivary glands and kidney compete for iodide but thyroid and kidney are the principal organs that compete for iodide.

The adult man requires 0.14 mg of iodide per day and an adult female requires 0.10 mg, growing children, pregnant and lactating women require more. The daily requirement is met by balanced diet and drinking water, exception being hilly areas where food and water may be deficient in iodine.

## **FORMATION AND SECRETION OF THYROID HORMONES**

The principal hormones secreted by the thyroid are thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>), T<sub>3</sub> is also formed in the peripheral tissues by deiodination of T<sub>4</sub>. Both hormones are iodine-containing amino acids. Small amounts of reverse triiodothyronine (3,3', 5'-triiodothyronine. RT<sub>3</sub>) and other compounds are also found in thyroid venous blood. T<sub>3</sub> is more active than T<sub>4</sub>. The naturally occurring forms of T<sub>4</sub> and its congeners with an asymmetric carbon atom are the L isomers. D-Thyroxine has only a small fraction of the activity of the L form. T<sub>4</sub> and T<sub>3</sub> are synthesized



in the colloid by iodination and condensation of tyrosine molecules bound in peptide linkage in thyroglobulin. This glycoprotein is made up of two sub-units and has a molecular weight of 6,60,000. Thyroglobulin is synthesized in the thyroid cells and secreted into the colloid. The hormones remain bound to thyroglobulin until secreted. When they are secreted, colloid is ingested by the thyroid cells, the peptide bonds are hydrolyzed, and free T<sub>4</sub> and T<sub>3</sub> are discharged into the capillaries. Thyroglobulin enters the blood as well as the colloid. The normal serum thyroglobulin concentration in humans is about 6 ng/mL, and this level is increased in hyperthyroidism and some forms of thyroid cancer.

**The synthesis of thyroid hormones is divided into four steps:**

**1. Iodine trapping**

The thyroid traps the plasma iodine in the inorganic form. It is essentially an active process by an active iodide transporter, Na<sup>+</sup>/I<sup>-</sup> symportor and stimulated by TSH. It is competitively inhibited by Thiocynates and perchlorates.

**b). Organification of thyroglobulin**

The inorganic iodide is oxidized to inorganic iodine at the thyroid follicular cells with the help of an enzyme peroxidase.

Iodine combines with amino acid tyrosine in the thyroglobulin molecule within the follicular cells to form monoiodotyrosine and diiodotyrosine (MIT and DIT). This process is inhibited by Thiouracil group of antithyroid drugs and by PAS and chloroquine.

#### **c). Coupling reaction**

Thyroxine (T<sub>4</sub>) is formed by coupling of two molecules of DIT and triiodothyronine (T<sub>3</sub>) by coupling of one molecule of each MIT and DIT. The coupling reaction occurs at the Thyroglobulin molecule. They are oxidative reactions and need peroxidase enzyme.

#### **d). Hormonal release**

The follicular colloid containing thyroglobulin is taken by the way of pinocytosis by follicular cells to form colloid droplets, which then fuses with lysozyme to form “phagolysosome”, in phagolysosome the thyroglobulin is hydrolysed by protease enzyme to liberate T<sub>3</sub> and T<sub>4</sub> which diffuse through the base of follicular cells to enter the circulation.

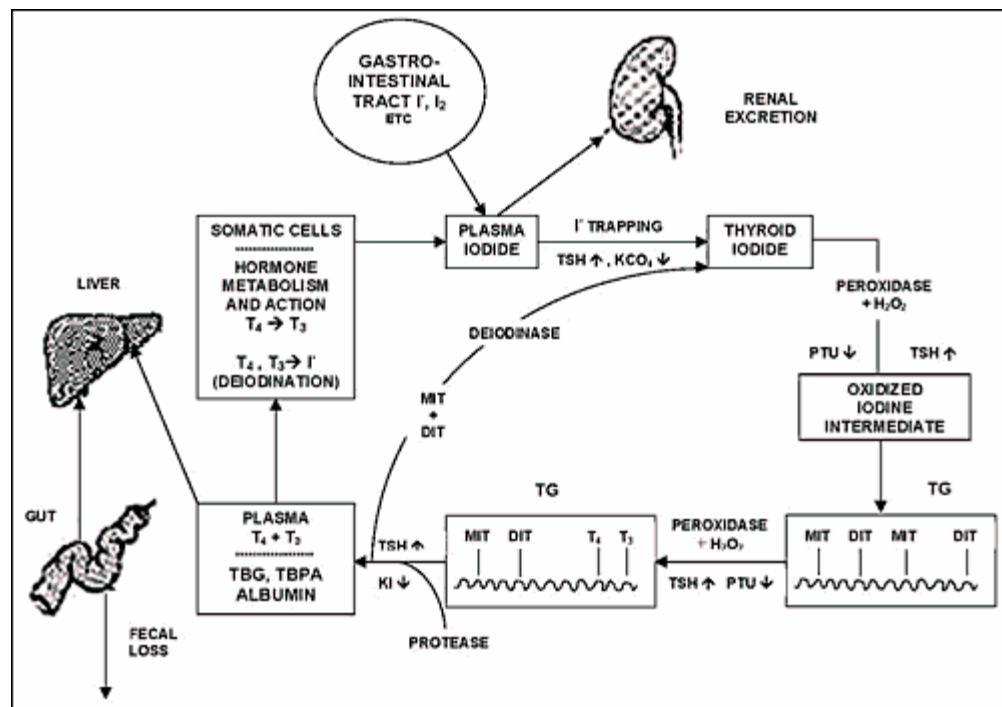
Inactive iodo-tyrosines liberated are acted upon by deiodinase enzyme to release the iodine which is reutilized by the cells to synthesize T<sub>3</sub> and T<sub>4</sub>.

## **KEY STEPS IN SYNTHESIS OF THYROID HORMONE**

1. Active uptake of iodide ( $I^-$ ) in exchange for  $Na^+$ .
2. Iodide may be discharged from the follicular cell by administration of competing ions such as perchlorate, bromide or chlorate.
3. Iodide uptake, the main control point for hormone synthesis, is stimulated by TSH.
4. Oxidation of iodide by hydrogen peroxide ( $H_2O_2$ ) to form active iodine. The reaction is catalyzed by thyroid peroxidase (TPO).
5. Active transport of iodine across the apical surface of the follicular cell.
6. Incorporation of active iodine into the tyrosine residues of thyroglobulin molecules to form mono- and di-iodotyrosines (MIT and DIT).
7. Uptake of the thyroglobulin into the lumen of the follicle and lining of iodinated tyrosine residues.
8. About 1% of stored colloid is removed each day. When the gland is very active this may rise to nearly 100% and colloid stores are depleted.

## SCHEMATIC REPRESENTATION OF THYROID HORMONE

### SYNTHESIS AND RELEASE



**Fig. 9** Thyroid Hormone synthesis

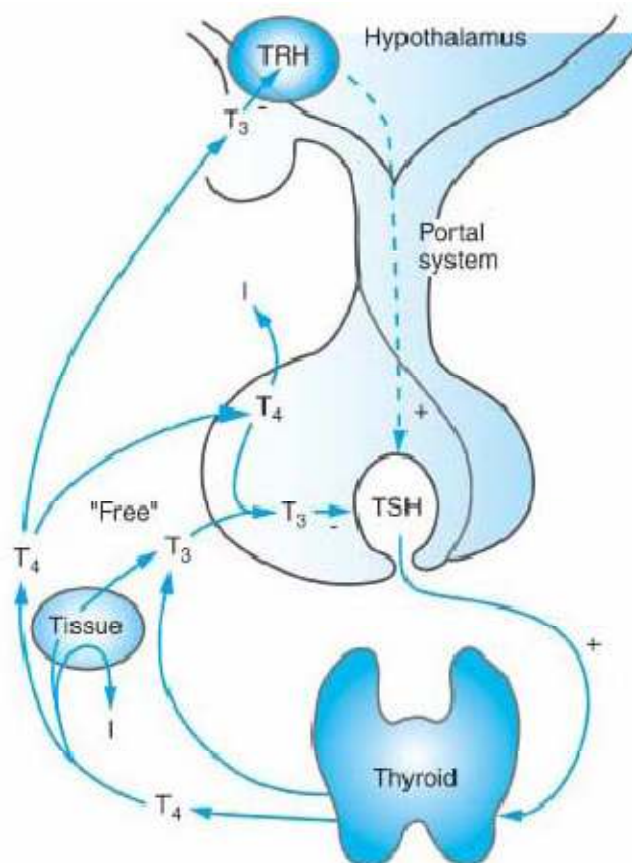
### REGULATION OF THYROID SECRETION

Thyroid function is regulated primarily by variations in the circulating level of pituitary TSH. TSH secretion is increased by the hypophysiotropic hormone TRH and inhibited in a negative feedback fashion by circulating free  $T_4$  and  $T_3$ .

Human TSH is a glycoprotein that contains 211 amino acid residues, hexoses, hexosamines and sialic acid. When TSH is

administered, thyroid function is stimulated. Whenever TSH stimulation is prolonged, the thyroid becomes detectably enlarged. Enlargement of the thyroid is called goitre. The negative feedback effect of thyroid hormones on TSH secretion is exerted in part at the hypothalamic level, but it is also due in large part to an action on pituitary, since T<sub>4</sub> and T<sub>3</sub> block the increase in TSH secretion produced by TRH. Infusion of T<sub>4</sub> as well as T<sub>3</sub> reduces the circulating level of TSH, which declines measurably within one hour.

**Fig 10. HYPOTHALAMO-PITUITARY AXIS FEEDBACK MECHANISM**



## **PATHOLOGY**

A single palpable nodule in otherwise impalpable thyroid gland is called solitary nodule thyroid.

### **FORMATION OF NODULES**

A loss of co-ordination between iodine metabolism, epithelial multiplication, thyroglobulin synthesis and colloid endocytosis are important in the genesis of nodule. Iodine deficiency and ingestion of goitrogens are the commonest cause of goitre formation. Iodine deficiency or goitrogens or hereditary factors lead to decrease in serum thyroid hormones with followed by increase in TSH which will produce diffuse hyperplastic goitre. The patient will become euthyroid because of normal thyroid hormone level, TSH level drops down and goitre disappears. If it persists after that it is a colloid goitre with inactive follicles. Because of fluctuation in TSH level, and varied response of cells to TSH, mixed active and inactive follicles are formed. In active follicles, because of high vascularity, haemorrhage occurs with central necrosis. Growth stimulating antibodies are also responsible for multinodular goitre. Patient is usually euthyroid. Firm painless nodules are palpable; hardness may be due to calcification. Pain & sudden increase in size may be due to haemorrhage and simulate malignancy.

Many thyroid disorders, both benign & malignant may manifest as solitary nodule.

## **SOLITARY THYROID NODULE**

### **Causes**

- |  |   |     |
|--|---|-----|
| 1. Dominant nodule in MNG                        | - | 50% |
| 2. Adenoma                                       | - | 20% |
| 3. Carcinoma (Papillary or follicular)           | - | 20% |
| 4. Cysts (colloid degenerative cyst, neoplastic) | - | 5%  |
| 5. Thyroiditis (Hashimoto's)                     | - | 5%  |

(Enlargement of whole of one lobe)

6. Lymphoma (rare)
7. Medullary carcinoma (rare)
8. Other Differential diagnosis of solitary Nodules

#### a. Infection

- Granulomatous
- Abscess

#### b. Developmental Anomalies

- Unilateral Lobe Agenesis
- Cystic hygroma
- Dermoid
- Teratoma

## CLINICAL EVALUATION

For proper management of STN, the three main prerequisites are

1. To make a correct diagnosis
2. To know when to operate
3. To know how to operate with minimal rate of complication

The usual presentation of the thyroid is an asymptomatic mass that is discovered by either the patient or the clinician. Upon initial contact a systematic inquiry of the patient's medical history is necessary. The goitre can cause two groups of symptoms

1. Those connected with the swelling in the neck and pressure or obstructive effect
2. Those related to the endocrine activity of the gland

So the clinician should have the knowledge of surgical anatomy and applied physiology of thyroid gland. The development of management strategy for the individual patient involves integration of information from a variety of possible sources including



1. History (Presentation)
2. Clinical examination (inspection -palpation -percussion - auscultation)
3. Investigation
  - a. Lab
  - b. Special
  - c. Biopsy

## **PRESENTATION**

### **A. SWELLING IN THE NECK**

- Lump at the junction of Isthmus & Lateral Lobe
- Obstructive symptoms (Dyspnoea - Dysphagia)
- Stridor, respiratory wheeze, engorgement of the neck veins, venous collateral vessels over the anterior chest wall (very large impacted retro sternal Solitary Thyroid Nodule)
- Painless, rapid development of thyroid nodule (malignancy)
- Pain in the thyroid gland with sudden enlargement of the nodule (Hemorrhage into dominant nodule in MNG or benign tumour or cyst.

- Pain in the thyroid gland with enlargement of the whole of one lobe (HASHIMOTO'S disease)
- Hoarseness of voice and inability to produce an explosive cough
  - Laryngeal nerve damage.
  - Unilateral vocal cord paralysis
- Horner's syndrome (Carcinomatous involving the sympathetic Nerve)

## **ENDOCRINE ACTIVITY**

### **B. ENDOCRINE ACTIVITY**

- Heat intolerance - weight loss & excessive appetite (with other signs of Hyperthyroidism)-TOXIC ADENOMA (Autonomous hot nodule)

## **PREVIOUS HISTORY**

During enquiry we can find out prior, low and high dose radiation exposure to head, neck and chest and the subsequent development of thyroid cancer. Between 1940 and 1960 large numbers of American children were exposed to low dose radiation therapeutically for variety of benign conditions such as tonsillar, adenoid hypertrophy and thymic enlargement and also high dose radiation to the cervical region in

neurosurgical practice. Review and screening of these patients after 20-30 years has revealed an unexpected high incidence of thyroid malignancy like papillary and mixed papillary carcinoma. Especially the findings of STN in an individual with the previous history of radiation exposure should be regarded with high suspicion for malignancy.

## **FAMILY HISTORY**

Papillary carcinoma of the thyroid has been reported within families but the rarer variety- medullary carcinoma is familial in approximately 20% of cases usually as an invariable component of MEN Type II syndrome associated with parathyroid adenoma and Pheochromocytomas.

## **EXAMINATION**

### **AGE & SEX**

Although over 80% of the STN arise in women, the malignant potential of a nodule in a man is approximately three times more. Malignancy is more likely in the nodule in children or teenagers or over the age of 60 years. In the great majority of patients the tumour is papillary or mixed papillary follicular type. Approximately two third of such individuals demonstrated palpable metastatic cervical lymphadenopathy and about 15% have pulmonary metastases.

Anxiety-related sinus tachycardia and, atrial fibrillation may suggest a diagnosis of hyperthyroidism. If the patient is hyperthyroid and has a STN, most probably diagnosis is solitary toxic nodule and it is a functioning autonomous thyroid nodule and causes toxicity in the older patient. The lesions are usually adenoma and on occasion adenomatous hyperplasia. The nodule is rare in children and such nodule in a child must raise a higher concern of its being malignant.

### **PRESSURE EFFECTS**

- Dyspnoea is due to compression and deviation of trachea in both benign and malignant condition of STN or due to extension of the growth into the trachea
- Dysphagia occurs late in the course of disease
- Dysphonia - due to involvement of Rec.Lar.nerve or Vocal cord.
- Pressure on the sympathetic chain produces Homer's syndrome and very rarely vagus nerve may be infiltrated as indicated by bradycardia. Pressure on the internal jugular vein or innominate vein and obstruction of the venous return of the head and neck sometimes produce edema of the face
- No examination of the thyroid gland is complete without careful palpation of lateral side of neck for lymphadenopathy. Clinical

enlargement of the nodes along the line of the ipsilateral jugular chain is strongly suggestive of metastatic spread from a primary thyroid carcinoma. This is particularly common in young people with papillary carcinoma

## **CLINICAL FEATURES**

- A Solitary nodule confined to one lobe and not visible or palpable thyroid lobe on opposite side (TRUE STN)
- Nodule moves on swallowing unless it's a large impacted restosternal nodule or malignant invasion or severe thyroiditis
- Tracheal deviation to one side
- Solitary nodule, hard in consistency, irregular with enlargement of ipsilateral cervical lymph nodes (Malignancy)
- Nodular shape-size more than 4 cm and fixation of adjacent skin and soft tissue to rule out extra glandular invasion
- The Carotid artery is displaced and less felt (carotid sheath involved: BERRY'S SIGN)
- Young lady with solitary nodule and palpable ipsilateral lymph nodes discrete, rubbery or firm and mobile (Papillary ca)

- In elderly patient, a rapid enlargement of thyroid lump (Follicular Ca. or Thyroiditis, Lymphoma or Anaplastic Ca.)
- Hashimoto's thyroiditis - one lobe firm to hard in consistency with reactive enlarged Lymph node
- Unilateral vocal Cord palsy due to recurrent laryngeal nerve involvement is almost due to thyroid carcinoma in a patient with STN or due to extension of the growth into the trachea. But rarely occurs with benign thyroid nodule lesions because of stretching or compression of the nerve

## **INVESTIGATION**

### **LABORATORY EVALUATION**

1) A complete blood count and ESR can be obtained if the clinician suspects an inflammatory or infectious thyroiditis. A thyroid peroxidase antibody assay is useful for the diagnosis of Hashimoto's thyroiditis. The diagnosis of Hashimoto's thyroiditis does not decrease the risk for malignancy but in fact, there is a higher incidence of carcinoma and lymphomatous lesions in these glands.

2) Laboratory analysis is an essential part of the evaluation. These measurements are complementary because none of the available ones,

except for possible calcitonin assay, is an accurate predictor for malignancy. The laboratory values most commonly obtained include thyrotropin (TSH),  $T_4$ , and  $T_3$ ; thyroglobulin, thyroglobulin antibody, erythrocyte sedimentation rate, thyroid peroxidase antibody (TPO antibody, microsomal antibody), CBC, and calcitonin.

3) The functional status of the thyroid gland has to be evaluated when working up a solitary thyroid nodule. A total  $T_4$  and total  $T_3$  levels are often obtained during the initial clinical visit. Their levels can fluctuate based on the circulating level of thyroid-binding globulin levels. A more accurate assay is the free  $T_4$  level, which correlates better with the activity of thyroid hormones in the body now a days.

4) Free  $T_4$  and  $T_3$  are measured routinely in many advanced centers because of the problem of high  $T_4$  and  $T_3$  values found in patients with increased level of binding proteins (TBG) This is most often due to estrogen (Pregnancy or oral contraceptive pill) which induce increased production of TBG by the liver. A more useful assay is the high-sensitivity thyrotropin assay (TSH), This assay is the only test that is necessary to detect abnormalities in thyroid function.

5) TSH level in peripheral blood is an important and wisely used parameter, particularly useful in hypothyroidism when the level is elevated. Serial measurement in the course of  $T_4$  therapy is essential to

ensure correct replacement. TSH level will be fully suppressed in primary, secondary or autonomous thyrotoxicosis

6) A thyroglobulin level can also be obtained. Many factors exist that may produce falsely elevated or decreased levels. Some of these factors include the degree of thyrotropin receptor stimulation, the volume of the gland itself, the presence of thyroid inflammation, injury to the gland (radiation, hypoxia, hemorrhage, biopsy, or surgery), multinodular goitre, decreased renal clearance, tobacco smoking, and estrogen level. One of the major limiting factors of the serum thyroglobulin assay is the presence of thyroglobulin antibodies. They may be present in up to 10% of normal subjects and in approximately 15% to 30% of patients with differentiated thyroid cancers. Thyroglobulin antibodies are present in 100% of patients with Hashimoto's thyroiditis and in between 89% to 98% of patients with Grave's disease. Benign and malignant conditions can produce elevated levels of thyroglobulin. A preoperative assay cannot be used to diagnose or exclude cancerous lesions and is probably not relevant when evaluating a thyroid nodule. The best use of this is in the follow-up of patients with thyroid cancer after thyroidectomies

7) Calcitonin is a valuable serum marker for medullary cancer. The test is important in screening the relatives of a patient with known medullary cancer. Although not used routinely, calcitonin level should be



considered in high-risk patients, such as patients with familial medullary thyroid carcinoma or multiple endocrine neoplasia. Recent studies advocated the routine use of calcitonin assay, followed by a pentagastrin-stimulating test if an abnormal calcitonin level is detected in the evaluation of patients with nodular diseases. A routine calcitonin level may allow identification of this aggressive tumour at an earlier stage. (Microscopic tumors without nodal metastasis)

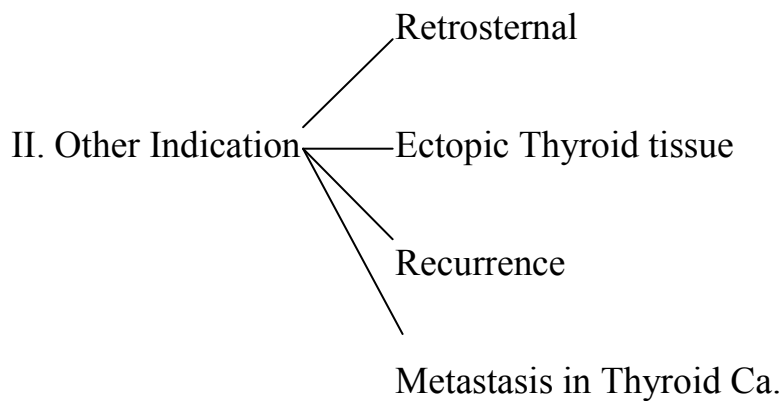
8) A survey that was conducted by the American Thyroid Association in 1998 showed the diagnostic trend of endocrinologists in North America. In this survey, a fictional patient with a 2 cm x 3 cm solitary nodule was presented. Ninety-nine percent of physicians obtained a thyrotropin level. Sixty-one percent also included a serum T4 or free T4 level. Thyroid peroxidase antibodies were obtained by 36% of respondents. Thyroglobulin antibodies, thyroglobulin level, and serum calcitonin were included in the initial work-up 18%, 4.9% and 5% of respondents, respectively.

### **Radioisotope imaging**

Nuclear scans of the thyroid, once the cornerstone of thyroid nodule evaluation, have fallen out of favor in the past few decades. Recent surveys by the American thyroid Association and the European thyroid Association showed that 23% and 66% of endocrinologists,

respectively, would still routinely obtain a nuclear scan in the evaluation of a solitary nodule.

I. I.e. Autonomous Toxic nodule to localize the area of Hyperfunction.



The most commonly used radioisotopes are technetium ( $^{99m}\text{Tc}$ ) and  $^{123}\text{I}$ . The choice of radioisotope is dependent on the preference of the clinician and radiologist, because they provide similar information.  $^{123}\text{I}$  is more physiologic than  $^{99m}\text{Tc}$ .  $^{99m}\text{Tc}$  quickly washes out of the thyroid gland before being organified inside the gland. The property of  $^{99m}\text{Tc}$  allows for a shorter scanning time (20-30 minutes) and the scanning over the thyroid can be performed immediately after intravenous the administration of  $^{99m}\text{Tc}$ .  $^{123}\text{I}$  imaging needs to be performed 24 hours after administration of  $^{123}\text{I}$  and the scanning time can run 4 to 6 hours in length. Radiation exposure is comparable for both agents, and is not significant, The whole body exposure from  $^{131}\text{I}$  and  $^{99m}\text{Tc}$  scanning is 0.04 c Gy and 0.07 c Gy, respectively. Imaging resolution is better with  $^{99m}\text{Tc}$  than radioiodine. Nodules that are smaller than 1 cm cannot be detected reliably by

either scan, as they are below the discriminating power of scintigraphic devices.

Approximately 80% to 85% of nodules are "cold" on scintigraphy, with 14% to 22% of them ultimately proven to be malignant. Five percent of nodules are "hot" with less than a 1% risk of malignancy. The remaining 10% to 15% are "warm or indeterminate nodules. It was suggested that these nodules harbor a higher risk of malignancy than "hot" nodules, with a reported range of less than 10% up to 36% [20,21]. Thus when grouping

- Cold Nodule - 80% - (Malignant - 20%)
- Hot Nodule - 5% - (Malignant - 1 %)
- Warm Nodule - 15% - (Malignant - 10%)

#### **D/D of cold nodule**

1. Cyst
2. Carcinoma
3. Throiditis
4. Benign Adenomas
5. Haemorrhage

"Cold" and "warm" nodules together, the sensitivity of scintigraphic scans for cancer diagnosis is 89% to 93%, but specificity is only 5% with a positive predictive value of only 10%.

Although scintigraphy does not offer any additional diagnostic value, it is a powerful adjunct test to more accepted modalities, such as FNA and ultrasound. The following circumstance would be indications for nuclear scans and its great value.

1. Outlining nodules and determining their studies (Hot, warm, cold).
2. Identification of a functional solitary thyroid nodule when initial serum thyrotropin is decreased.
3. If an FNA is reported as "follicular neoplasm" or "suspicious", the finding of a "hot" nodule decreases the suspicion of malignancy.
4. Retrosternal goitre especially in young women with chubby necks.
5. Intrathoracic extension of thyroid.
6. Recently, Thallium-201 scan was reported to be a useful diagnostic tool to differentiate between benign and malignant thyroid nodules.
7. Detecting neck metastasis.
8. Detection of pulmonary or other metastasis after ablation of the gland (Tracing and Therapy).

## **X-RAY**

X-ray chest including the neck (AP & lateral view) is useful.  
Calcifications in tumours are of two varieties.

- The common one is dense, well circumscribed
- The second type appears as fine grains of sand or as thin strands and can only be seen in those tumours which contain calcified "psammoma bodies"
- The other x-ray evidence includes invasion of trachea or esophagus (by barium swallow examination)
- Deposits in the lung may be discrete, well-defined rounded lesions. Spread to mediastinal glands occur in medullary carcinoma
- Pleural effusion may be present
- Bone deposits are osteolytic and occur in 60 - 70% of cases in ribs, spine & pelvis especially in follicular carcinoma and are usually pulsatile
- Some patients may present with pulsatile bone swelling in the scalp

## **CT AND MRI**

CT scans are a highly sensitive technique in detecting thyroid nodules. They have a very limited role in the initial management of a STN. CT scan can be helpful

- If the nodule occurs in a diffusely enlarged gland that makes palpation difficult
- CT scans are more useful in detecting thyroid tissues in the retro tracheal and retro clavicular region
- Assessment of mediastinal involvement and cervical lymphadenopathy MRI plays a minor role in the evaluation STN but it demonstrates exquisite soft tissue details and vascular anatomy
- This allows identification of extraglandular invasion and involvement of great vessels. An advantage of the MRI scan over the CT SCAN is the possible use of contrast (Gadolinium) without interfering with nuclear scintigraphy. A few studies investigated the use of MRI to study nodules in different functional status

## **BONE SCAN**

- To rule out Suspicion of secondary skeletal metastasis.

## **ULTRASOUND (HIGH RESOLUTION)**

Ultrasonography is the most widely used imaging technique for the evaluation of thyroid nodules. Modern ultrasound is performed with high frequency transducers (7-13 MHz) and can detect solid nodules of 3 mm to 4 mm and cystic nodules of 2 mm in diameter. When routinely used for solitary nodules, it can discover coexisting nodules in approximately 50% of patients. The routine use of ultrasound for solitary nodules was investigated by Marqusee et al at the Thyroid Nodule Clinic of Brigham and Women's Hospital. Ultrasonography changed the clinical management of 44% of patients who were referred for solitary nodules. The findings that altered management included the discovery of multiple nodules, no actual nodule identified, and very small solitary nodules (<1 cm). Based on their series, the investigators concluded that routine US should be seriously considered in the evaluation of solitary nodules.

Nodules can be solid or cystic on ultrasound. Purely cystic nodules are uncommon (-1%), with partially cystic lesions accounting for up to 20% of nodules. Cystic lesions were reported to carry a lower risk of malignancy (0.5% to 3%). Occurrence of papillary carcinoma in cystic or partially cystic thyroid nodule is well recognized. However, the discovery of a purely cystic nodule should not discourage a needle aspiration for cytological analysis. Predominantly cold nodules carry a higher risk of

malignancy (-10%). Many studies looked into the echogenic pattern of nodules to predict malignancy, but currently none of them has discovered a definitive pattern.

The characteristics that suggest a malignant nodule are described in Box 1: A hypoechoic signal is more typical of malignant nodule although many benign nodules also demonstrate hypoechogenicity. Benign nodules, such as adenomas, are generally surrounded by a well- defined capsule, and thus demonstrate a 'halo' sign on ultrasound. Calcium deposits can be fine, punctuate findings in papillary cancer that correspond with Psammoma bodies histologically, but can also be coarse and amorphous. Kakkos et al reported a series of 82 solitary thyroid nodules that were imaged with ultrasound and managed by surgical excision. Ultrasound showed that 22 patients had calcification in their thyroid glands, Histopathological slides were compared with preoperative US, They noted a malignancy incidence of 55% (12 out of 22) in patients with solitary nodules with calcifications versus 23% (14 out of 60) for patients with non calcified nodules. In another study, Thakashima et al reported a series of micro calcifications with a specificity of 93% and positive predictive value of 70% for cancer, albeit with a sensitivity of only 36%. Koike et al applied multiple logistic regression analysis on five different findings (margin, shape, echo structure, echogenicity, and



calcification) in a retrospective series of 329 nodules (all > 5mm) that were imaged with ultrasound. Patients then underwent thyroidectomies and US findings were correlated with histopathology. Two hundred and sixty-five patients had non follicular neoplasm and 64 patients had follicular neoplasm. Their sensitivity of preoperative diagnosis was 86.5% for patients with nonfollicular neoplasm, and 18.2% for patients with follicular neoplasm.

The specificity was 92% and 89% respectively,

An ultrasound is a safe, noninvasive, non-radioactive test that should be ordered judiciously. Recommendations for ultrasound are:

- Non-palpable or difficult to palpate nodules for US- guided FNA
- Assessment of regional lymph nodes (pre & Post Operative)
- Follow- up imaging for solitary nodules that are managed medically or by observation
- Non-diagnostic fine needle aspirate (as an adjunct to repeat FNA)

### **Box1. Ultrasound features suggesting malignancy**

1. Absent 'halo' sign
2. Solid or hypoechogenicity
3. Heterogeneous echo structure (Hypoechoic)
4. Irregular margin - Poorly defined margin
5. Fine calcifications
6. Extra glandular extension

### **Ultrasound features suggesting Benign**

1. Rim (Halo) around the nodule
2. Significant Cystic component
3. Hyper echoic nodule
4. Well - defined nodule margin
5. Peripheral egg shell like calcification

Routine use of US is probably not indicated at the time because of its cost, its subjective interpretation, and the existence of alternative diagnostic tools, such as FNA. The cytology analysis of the nodule still remains the gold standard, but features on ultrasound may provide the clinician with crucial information, especially when a needle aspirate is inconclusive. The best use of US as a diagnostic modality is combination with FNA.

### **FINE NEEDLE ASPIRATION AND CYTOLOGY**

Needle aspiration of the thyroid was pioneered in the 1930s by Martin. Scandinavian workers introduced fine needle aspiration. It eventually gained wide acceptance in the western world in the 1980s and is now used increasingly as a first line investigation of the patient with solitary thyroid nodules. FNA is a simple, relatively non-invasive procedure that provides extremely valuable clinical information. It is highly sensitive and specific test in diagnosis of thyroid cancer especially papillary carcinoma which forms 80 to 85% and in patients with medullary, lymphoid tumours and anaplastic carcinoma.

It is least valuable in distinguishing benign from malignant follicular and Hurthle cell neoplasms. FNA is performed with 10cc or 20 cc pistol syringes coupled with 22, 23 or 25 gauge needle. (Minimum 6 passes) Tissue sludge, tissue fragments and blood are aspirated and air-

dried smears are produced which are stained by May-Grunwald or Diff Quick- staining. Complications from FNA are neither significant nor frequent.

### **Box 2. Complications of FNA**

- Pain
- Hematoma
- Entry into trachea
- Transient thyroid swelling - cystic degeneration
- Transient Vocal cord paralysis
- Formation of calcification
- Necrosis of nodule - Capsular pseudo invasion Fibrosis
- Transient thyrotoxicosis
- Elevation of thyroglobulin level
- Seeding along the tract is extremely rare

Box 2 includes some of the potential complications. Reports of cytology need to be standardized. The four recognized categories of FNA are

1. Benign
2. Malignant
3. Suspicious (Atypical)
4. Insufficient (non-diagnostic)

### **I Benign Reports Includes (75%)**

- Follicular Adenoma (nontoxic & Toxic) - confirmed by histopathology
- Hyperplastic colloid nodule
- Thyroiditis
- Cysts

### **II Malignant Category Includes (5%)**

- Papillary -> (complex cyst is 72% malignancy)
- Medullary
- Lymphoma

- Poorly differentiated or undifferentiated Thyroid cancer (Anaplastic)
- Metastatic non-thyroid cancer from breast, lung, kidney

### **III Suspicious (10%) (Atypical)**

The most common cause of categorizing an FNA aspirate as "Suspicious" is the inability to differentiate a follicular adenoma from a well-differentiated follicular carcinoma because one is unable to visualize the capsule and vascular invasion. Some of the other possible causes of a "Suspicious" report are as follows.

- Follicular neoplasm
- Hurthle cell neoplasm
- Follicular variant of papillary carcinoma
- Low-grade papillary carcinoma
- Hyalinizing trabecular adenoma
- Hashimoto's thyroiditis with metaplasia
- Any cancer with sub optimal sampling
- Adenomatous goitre with microfollicular structure predominance

#### **IV Insufficient (Non diagnostic)**

The highest rates of "Non-diagnostic" reports are found in cases with multiple calcifications, small nodule (< 1cm) and necrosis among others. "Nondiagnostic" reports are caused by the lack of cellular components in the aspirate or because of improper handling of the specimen. An adequate smear consists of at least five to six groups of follicular cells, with each group containing at least 10 cells; pseudocysts are believed to occur in cancerous and benign nodules at a rate of 23% to 33% and 27% to 35%, respectively. Repeat FNA, ultrasound-guided FNA, or excision is recommended in patients with cystic nodules.

#### **CORE NEEDLE BIOPSY**

##### **Indication :**

- Anaplastic Ca.
- Lymphoma Employing a needle of true-cut type and carried out under local anesthesia is occasionally of value in establishing a diagnosis in the patient with a large, often hard and fixed mass in the neck. Core biopsy produces a small cylinder of tissue, which is then submitted to histopathology, not cytological examination. Because of risk of hemorrhage and injury to adjacent structures like

trachea, there is no place for large needle biopsy of this type in the routine assessment of the STN.

## **ROLE OF FROZEN SECTION**

- It is used for Atypical solitary thyroid nodule after getting inconclusive.
- FNAC report especially Follicular and Hurthle Neoplasm
- Recent studies in John Hopkin, Medical college of Georgia Rush Medical College, Chicago have reported that 80% of Frozen section rendered no useful information because of difficulty to identify the capsular & vascular invasion and 5% gave inaccurate result
- In atypical STN, its advisable to resects the lobe with isthmus
- Treat according to the post operative Histopathology report



## THYROID INCIDENTALOMAS<sup>38</sup>

*Incidentaloma* is used to refer to a lesion which is detected during unrelated procedure or an investigation, and it can be surgical or radiologic. Incidentalomas of thyroid refer to thyroid lesions discovered during radiologic investigations which are unrelated to thyroid gland. Due to increasing use of such imaging, prevalence of such lesions will most probably increase, and their management will be controversial.

Thyroid nodules are very common, detected by palpation in 4% to 7% of population and in about 60% patients during postmortem examination. In 2004, a study was done to detect thyroid nodule prevalence incidentally during carotid doppler scanning and in 9.4% of ultrasound examinations, 1 or even more nodules were identified. Other numerous studies identified incidental thyroid nodules during unrelated diagnostic tests, which included computed tomography (CT), then positron emission tomography (PET), and also nuclear scintigraphy.

In another study by Papini et al in 2002, thyroid cancers were identified in 9.2% of the solitary nodules and 6.3% of the multinodular goitres.<sup>8</sup> During surgery, 35.5% of such lesions showed extracapsular growth and 19.4% cases showed lymph nodal involvement.

Many other studies said that prevalence of the thyroid cancers in an incidental impalpable thyroid nodule was similar to that seen in palpable

thyroid nodules. But, overt thyroid cancer is a rare malignancy, which constitutes only 1% of all the malignancies.

Most common type of thyroid cancer detected in FNAC or surgery was the papillary carcinoma. Papillary carcinomas which are less than 1 cm are called “microcarcinomas” and they can be incidentally detected in almost 36% postmortem examinations.

In a large retrospective study, although prevalence of thyroid carcinoma was almost double during the period (especially papillary), the disease mortality was stable. Based on this finding, authors said increased use of the ultrasound and USG guided FNA will increase identification of subclinical papillary carcinoma. But such small primary cancers may be associated with metastatic lymph node diseases<sup>2</sup>, with some histologic subtypes like tall cell or otherwise columnar types, especially at risk.<sup>14</sup> Hence , it looks like papillary microcarcinomas are more frequent and indolent, and in certain cases alone, they act aggressively, even if less than 1 cm.

According to a study by Kang et al in 2004, the prevalence of thyroid incidentalomas was 13.4%. The malignancy rate within thyroid incidentalomas was 28.8%. There were no significant differences in age, nodule size and number, thyroid function test, and Tc99m thyroid scan between benign and malignant incidentalomas. US characteristics of solid echostructure, irregular margin, and calcification showed meaningful

diagnostic value in detecting malignancy in thyroid incidentalomas . Most malignant incidentalomas were low stage. In conclusion, occult thyroid cancers are a fairly common finding. There were no significant differences in clinical and laboratory parameters between benign and malignant thyroid nodules <1.5 cm; however, US findings can be used in the decision of optimal management strategies.

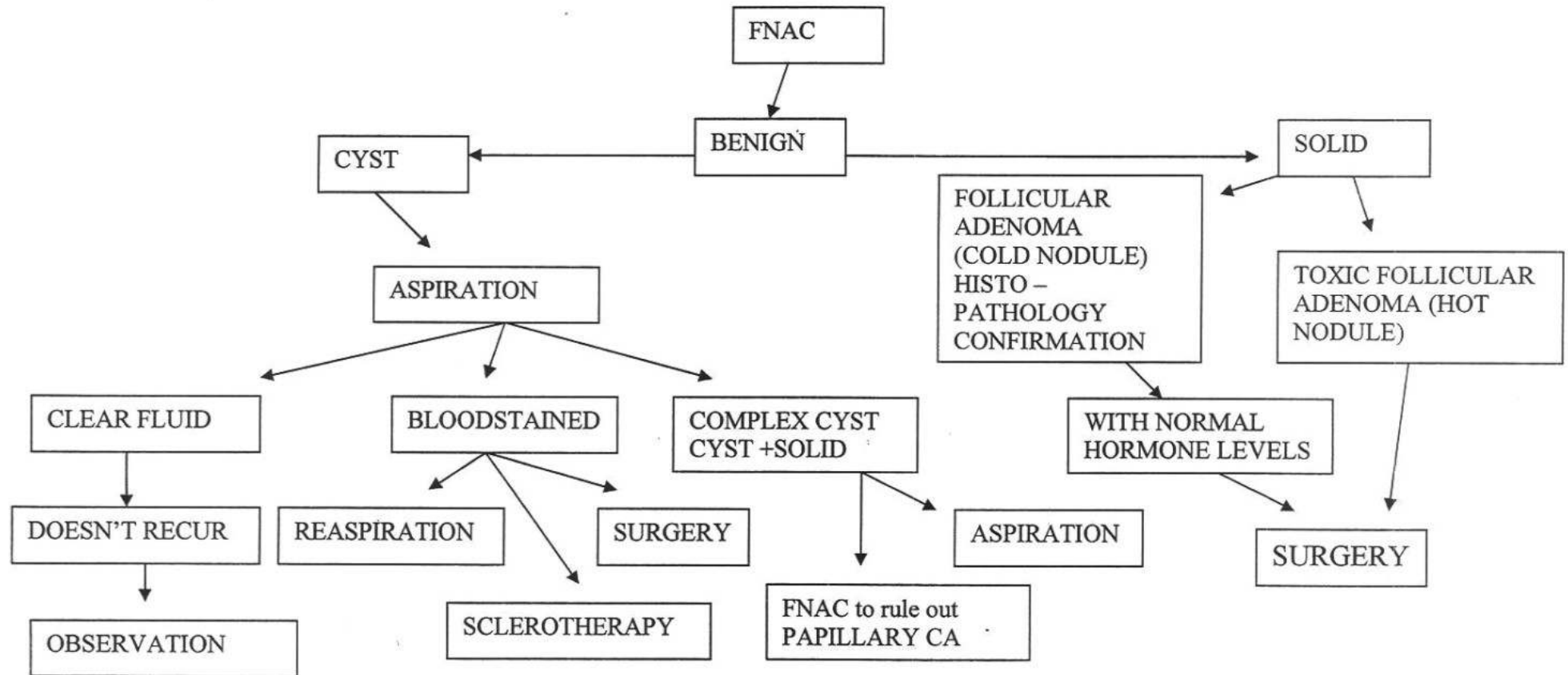
## **MANAGEMENT OF SNT**

The challenge of management of a SNT is to differentiate between benign and malignant neoplasms. The management option for benign condition is surgical or non surgical. Surgery should be advised after fine needle aspiration of STN and cytology in the following conditions.

- SNT in younger than 20 or older than 60 yrs
- Malignant potential of nodule in men is more
- Previous radiation to the cervical region
- Strong family history of thyroid cancer
- Malignant nodules
- Cytological diagnosed follicular neoplasm
- Cystic nodules which occur following aspiration

- Suspicious (ATYPICAL) category of FNAC
- SNT with pressure effect- compressive infiltrative and invasive features causing recurrent nerve palsy
- Cervical metastasis
- Large nodule (>4cm)
- Rapid growth with pain
- Growth despite thyroid suppression therapy
- Solitary cold nodules, solid or nearly solid by ultrasonography or when needle biopsy is inconclusive.

## I MANAGEMENT OF BENIGN STN



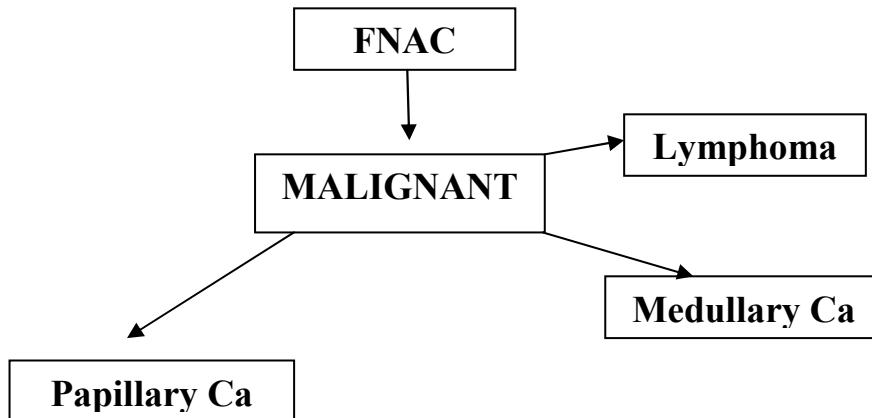
Observation

Hemithyroidectomy with isthmus

**MANAGEMENT OF SOLITARY THYROID NODULES**  
 Trial – permanent cure by instilling tetracycline 100 mg/ml 0.9% saline or injection of absolute alcohol

After aspiration 1 ml to 2 ml of preparation was instilled into the cyst cavity

## II MANAGEMENT OF MALIGNANT SNT



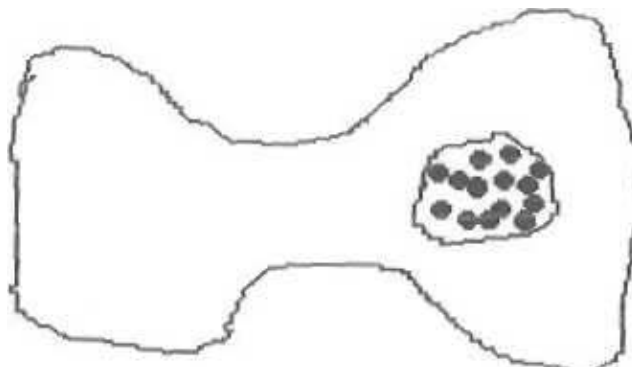
### PAPILLARY CARCINOMA

#### Best current Method

- FNAC-1<sup>st</sup>
- Pre operative Assessment of Lymph Nodules in the neck(clinical & by high resolution ultra sound)
- Then expose the gland and proceed

#### 1. (STN) TUMOUR CONFINED TO ONE LOBE -

#### MULTIFOCAL LESION NO LYMPHNODE INVOLVEMENT



- **TREATMENT:**

- Total thyroidectomy or near total thyroidectomy (Involved Lobe -> Total lobectomy + contra lateral Lobe -> Lobectomy .Leaving the post. Capsule to protect Rec. Larynx. Nerve and parathyroid. 1-2gm of thyroid tissue, should be left and it helps to preserve blood supply to Parathyroids

- Why total & not Hemithyroidectomy?

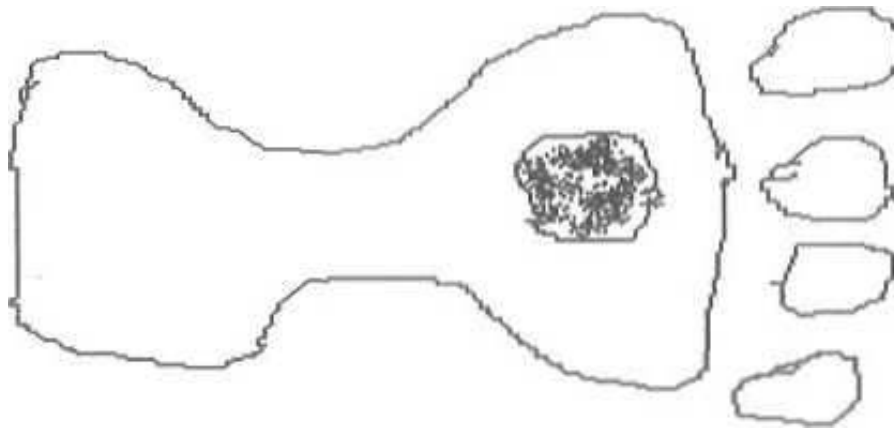
- Due to early intraglandular lymphatic invasion, the chances of opposite lobe involvement is more than 30%

- Post operative-TSH Suppressive Therapy as it is TSH dependent tumour

- Follow Up

## **2. (STN) TUMOUR CONFINED TO ONE LOBE + LYMPH NODES INVOLVEMENT IN THE SAME SIDE**

- Lymphadenopathy - by clinical examination
- Identified LNS by imaging
- Biopsy-excision L.N
- During surgery frozen section-Biopsy



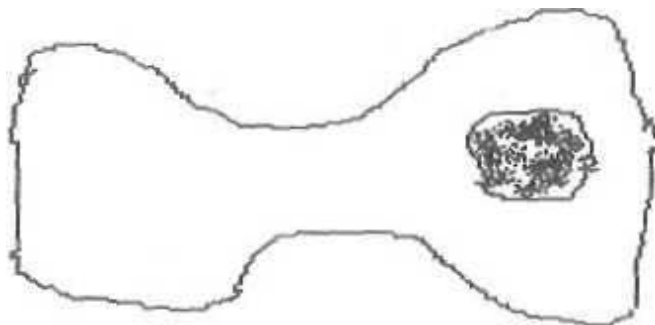
### **PRESENT ADVICE:**

- Total Thyroidectomy
- Central neck nodes dissection
  - Including Ipsilateral trachea- Oesophagic groove o Pretracheal area
  - Along the Recurrent laryngeal nerve and Inferior thyroid vein o Anterior mediastinum
  - If Lymph nodes are involved in the lateral Triangle, Functional Block Dissection (MRND) is added
- Presently all the patients who undergo total thyroidectomy for carcinoma of size >1.5 cm should be considered for <sup>131</sup>I ablation treatment



- If residual tumours is present external radiotherapy to thyroid bed, neck, Lymph node and upper part of the mediastinum is recommended
- Post operative TSH Suppressive therapy - The average daily dose (0.25-0.3mg)
- Follow up

**3. (SNT) TUMOUR CONFINED TO ONE LOBE+ NO LYMPHNODES**



## **CURRENT SURGICAL PROCEDURE:-LIMITED SURGERY**

- Total thyroid Lobectomy on the same side of the lesion
- Resection of the Isthmus
- Further excision of 60% of the grossly unaffected lobe by leaving sleeve of the contra lateral lobe
- Post operative. TSH Suppressive therapy [Current data suggests that 20% SNT do respond to Thyroid Hormone suppressive therapy]
- Prognosis is good in Low risk patient
- Follow Up

## **FOLLICULAR CARCINOMA**

- Presents rarely as SNT and the surgical treatment is controversial
- Treatment SNT in a Low risk patient (AMES)
  - Male- less than 40 yrs
  - Female -less than 50 yrs
  - No distant Metastasis

- Minor invasion of capsule with no vascular involvement
- The size of the tumour less than 5 cm

### **LIMITED RESECTION**

- Total thyroid lobectomy on the same side of the lesion
- Resection of the isthmus
- Leaving sleeve of the contra- lateral lobe (Hemi-thyroidectomy + isthmusectomy are good enough procedure)
- Follow up

If histopathology report reveals extensive vascular & capsular invasion

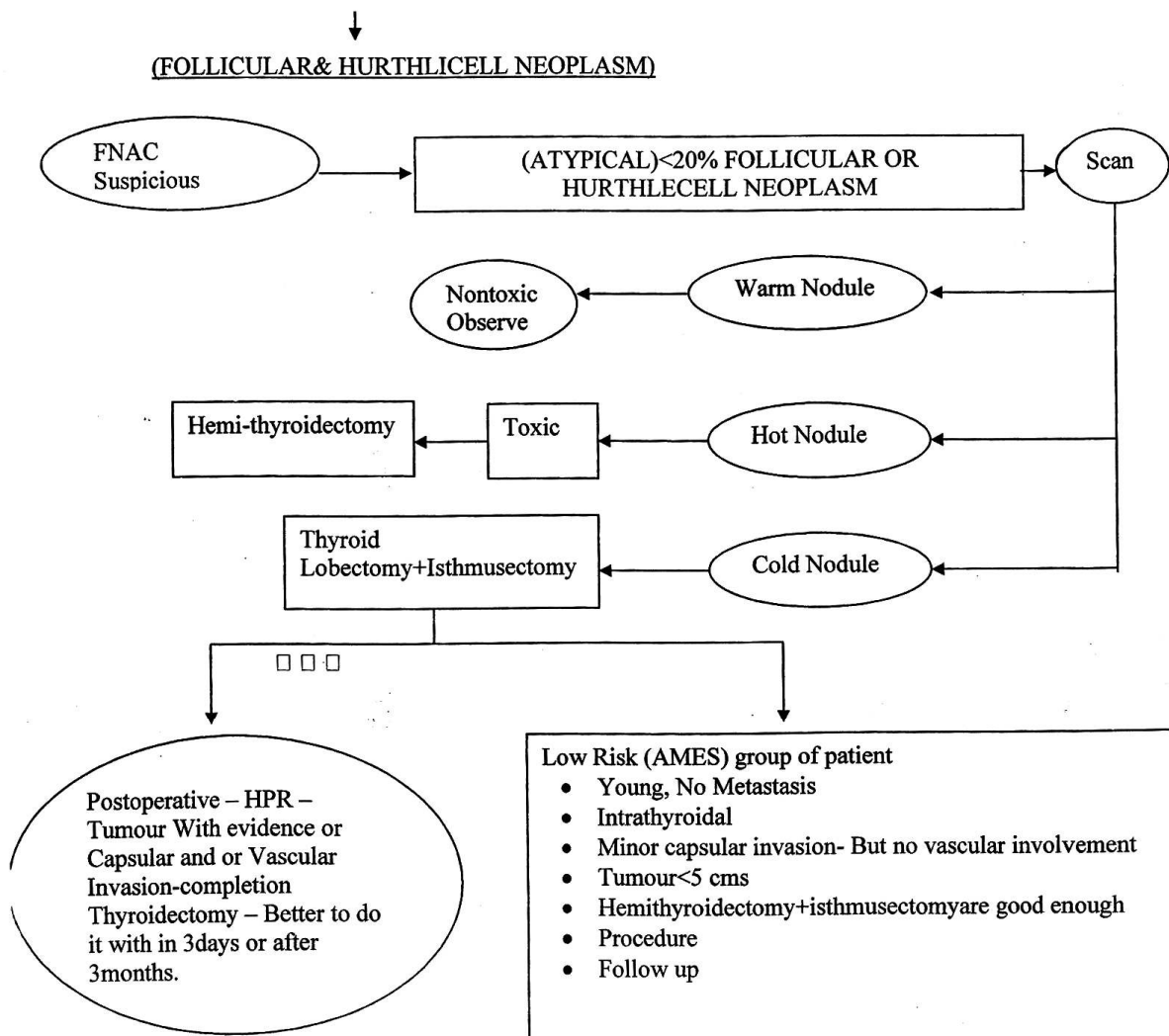
- Completion thyroidectomy is indicated
- Post operative Radio Iodine Tracing and Treatment (Ablation)
- Thyroxin (0.25 - 0.3 mg daily) as TSH suppressive docs
- Follow up

## MEDULLARY CARCINOMA (Rare)

If Medullary Carcinoma presents as SNT- total thyroidectomy & central Lymph node dissection from hyoid to innominate vein and laterally to Jugular Vein. Lymph node lateral to the internal jugular vein is sampled and if positive in frozen section biopsy, formal modified radical neck dissection should be carried out.

### III MANAGEMENT OF SUSPICIOUS (Atypical)

#### (FOLLICULAR & HURTHLE CELL NEOPLASM)



#### **IV. INSUFFICIENT OR NON-DIAGNOSTIC**

The last category of FNA result is the "nondiagnostic" for "insufficient of diagnosis" reading. When this result is obtained, a repeat FNA is performed, possible with ultrasound guidance to increase the yield. Carmeci et al reported that the rate of insufficient sampling decreased from 16% to 7% when ultrasound guidance was used. Despite repeated aspirations, a small group of patients will still have nondiagnostic FNAs. It is acceptable to have clinical follow-up, with surgical intervention only when poor prognostic indicators are present. In this situation, the management should be tailored to the individual patient.

The main goal of FNA is to accurately predict which nodule is malignant and which is benign

- Overall accuracy is estimated 92%-95%
- False positive rate is approximately 0,8%-9%
- False negative rate is 5%
- One of the most common causes of a false negative reading is Cystic nodules especially when larger than 3 cm
- Pseudocysts are believed to occur in cancerous and benign nodules at the rate of 23% to 33%. Repeat FNA, ultrasound guided FNA or excision is recommended in patients with cystic nodules

## **NON - SURGICAL TREATMENT**

- When the question of malignancy within an isolated thyroid nodules has been eliminated by FNA and cytology, and in the absence of obstructive symptoms it is reasonable to offer the patient a conservative management plan
- Though not proven by constant believable results from studies— TSH suppression by exogenous T4 has been practiced in the assumption that benign tumour will regress or stop growing while carcinoma may continue to grow ,since benign lesions are more TSH dependent. On average 16% of malignant-22% of Benign lesions were suppressible
- Administration of suppressive dose of thyroxin therapy 50-100mcg /day is acceptable for patient with benign STN. If the swelling recurs surgery is indicated
- If FNA shows Lymphocytic thyroid, thyroxine is likely to help especially if TSH is above normal whereas colloid nodule this treatment is unlikely to succeed

## **KEYFACTS**

- FNAC is now used as a first line investigation in patients with solitary nodule and it is considered the gold standard diagnostic test
- Solitary thyroid nodules are common entities and the majority of these are benign. The surgical treatment of thyroid cancer is controversial
- True solitary thyroid nodules are considered malignant until proved Benign, especially in young patient and elderly
- A dominant nodule in multinodular gland is considered benign unless some finding is suggestive of malignancy (Laryngeal nerve palsy, enlarged lymph nodes)
- Hemithyroidectomy with resection of isthmus in continuity seems a safe and good enough procedure and the complications are minimal
- In limited resection
  - Recurrence is treatable
  - Favorable prognostic group patients has equal survival both with limited and radical resection

- Less complication like hypothyroidism and rec. laryngeal palsy, comparing total thyroidectomy
- Ultrasound and nuclear scans are also useful tests, but are best used in conjunction with FNA. Clinical decisions are often based on the results of the FNA



## **MATERIALS AND METHODS**

This is a prospective study of randomly selected patients with clinically palpable, solitary nodule thyroid diagnosed and treated at PSG Institute of Medical Sciences and Research. Total duration of study was eight months, from February 2014 to September 2014. A total of 30 patients were selected.

Each patient's symptoms and signs were entered in a proforma (given at the end of the dissertation) with clinical examination in relation to the thyroid swelling and lymph node involvement and a routine systemic and general examination was done.

All the patients were subjected to basic investigations like complete hemogram, Blood sugar, urea, urine analysis, chest radiogram and neck radiogram. Tissue diagnosis was obtained by fine needle aspiration cytology in all these patients.

Thyroid profile was done in all patients with solitary nodule thyroid. Radioiodine study was not done since the facility was not available at our hospital. Ultrasound of neck and Computed Tomogram scan of, chest and skull were done in selected patients. All operated specimens were subjected to histopathological examination.

Preoperative and postoperative complications were analysed. Most cases were regularly followed up throughout the study period. All the observations were analysed and compared with other studies.

#### **INCLUSION CRITERIA:**

- All patients undergoing surgery for solitary thyroid nodule
- Both toxic and non-toxic solitary thyroid nodule

#### **EXCLUSION CRITERIA:**

- Recurrent thyroid nodule
- Diffuse hyperplastic goiter

#### **THYROIDECTOMY PROCEDURE**

##### ***For Hemi thyroidectomy***

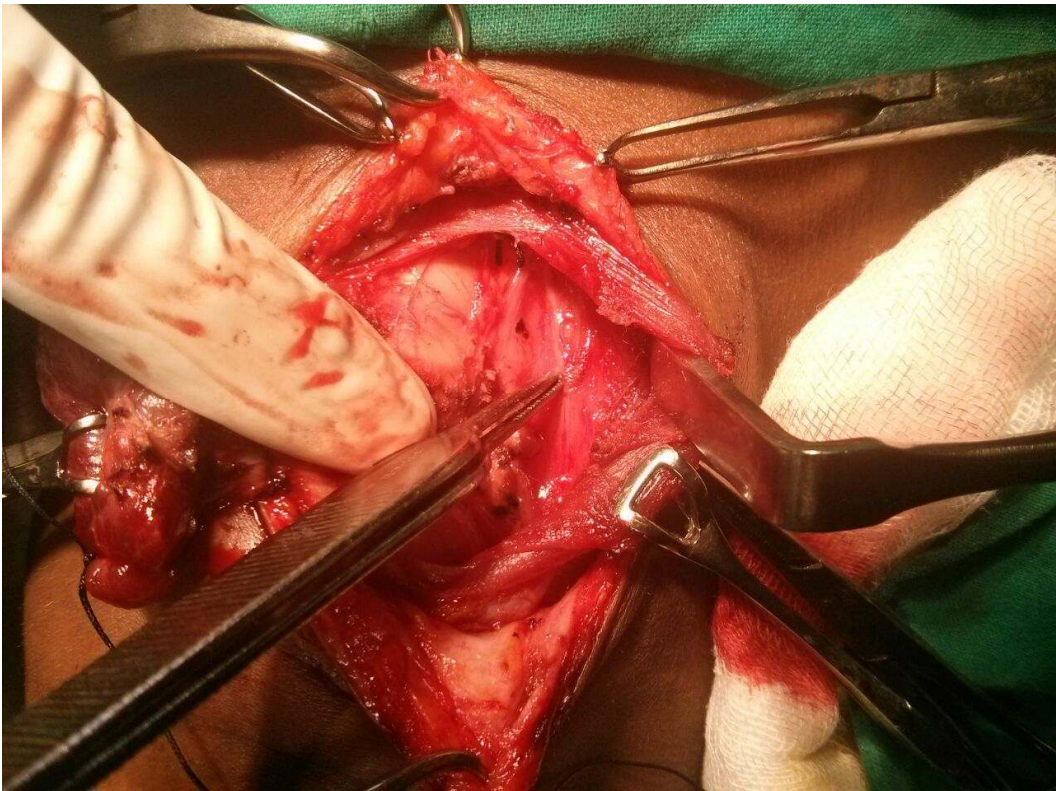
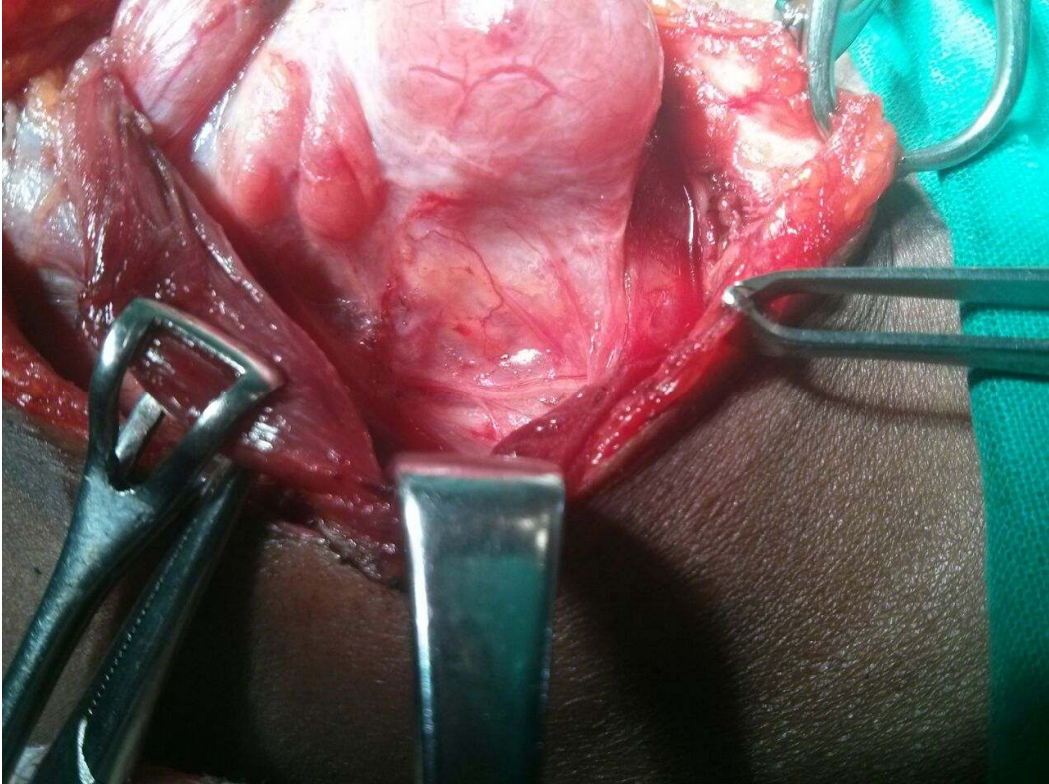
1. Patient in supine position, neck extended with the help of a sandbag placed between the shoulders and rotation of the head is avoided by keeping the head on a ring.
2. A transverse collar incision is made about two finger breadth above the clavicle.
3. Elevation of upper & lower flaps in the plane between platysma and deep cervical fascia.
4. Vertically incise the deep cervical fascia in the midline.
5. Vertically split infrahyoid muscles.

6. Ligate and divide middle thyroid vein.
7. Ligate and divide superior thyroid pedicle
8. Inferior thyroid artery to be ligated in continuity away from the gland.
9. The thyroid isthmus is clamped at the junction with contralateral lobe and divided.

***For total thyroidectomy:***

The same technique to be followed on contralateral side also. The parathyroids are carefully separated and left insitu.

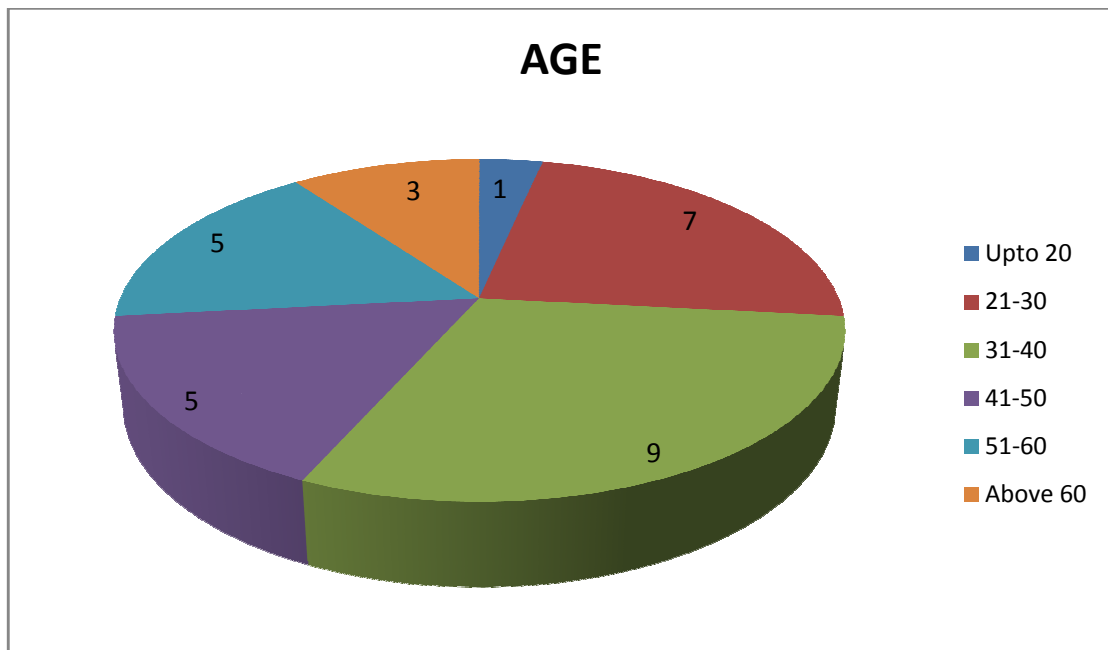
## INTRA OPERATIVE PICTURES



## OBSERVATION AND RESULTS

**TABLE:1**  
**AGE DISTRIBUTION**

AGE IN YEARS	NO. OF PATIENTS	PERCENTAGE
UPTO 20	1	3.33%
21-30	7	23.33%
31-40	9	30%
41-50	5	16.67%
51-60	5	16.67%
ABOVE 60	3	10%

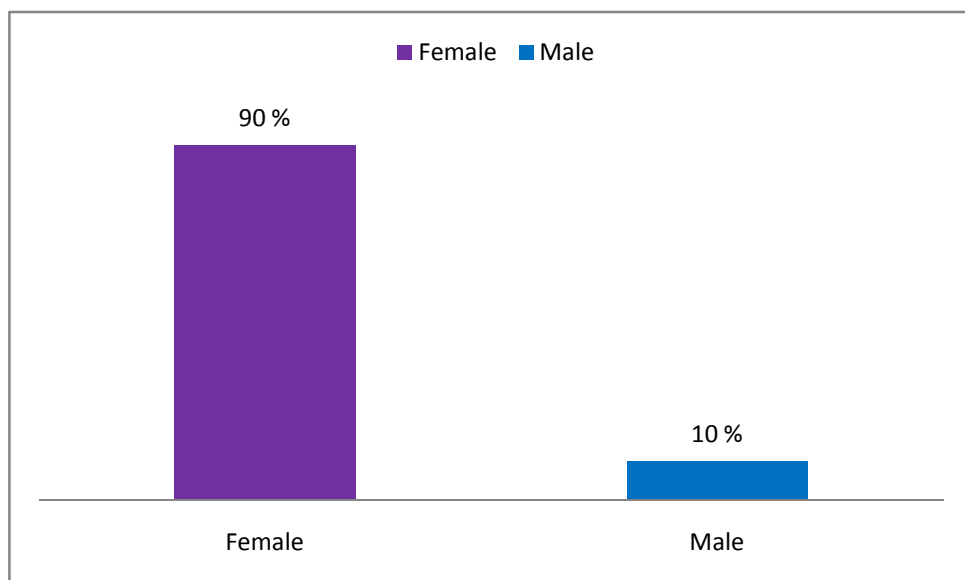


In this study the youngest patient was 17 years old and the oldest was 65 years old. The peak incidence is 2<sup>nd</sup> and 3<sup>rd</sup> decade. 75% of

solitary nodules occurred during the age between 21-60 years. The highest incidence of 30 % was recorded during the 3rd decade of life.

**TABLE : 2**  
**SEX DISTRIBUTION**

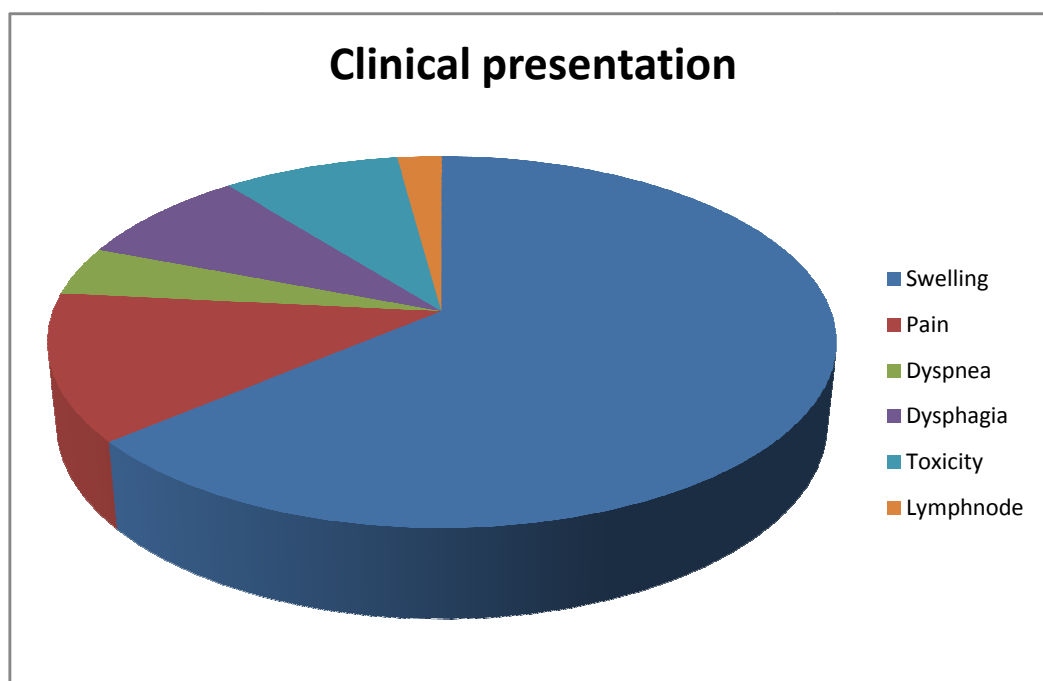
SEX	NUMBER OF PATIENTS	PERCENTAGE
Male	3	10 %
Female	27	90%



There is a marked preponderance of female patients, who constitute about 90% of cases. The female to male ratio is 9:1. This distribution is in accordance with most of the reported series in our country and elsewhere. Considering the total number of admissions of any thyroid swelling the female incidence is more partly because of increased prevalence and partly because of increased cosmetic awareness among young females.

**TABLE-3**  
**CLINICAL PRESENTATION**

<b>Clinical presentation</b>	<b>No. of patients</b>	<b>percentage</b>
Swelling in thyroid region	30	100%
Pain	6	20%
Dyspnoea	2	6.67%
Dysphagia	4	13.33%
Toxic symptoms	4	13.33%
Hypothyroid symptoms	6	20%
Cervical lymphadenopathy	1	3.33%



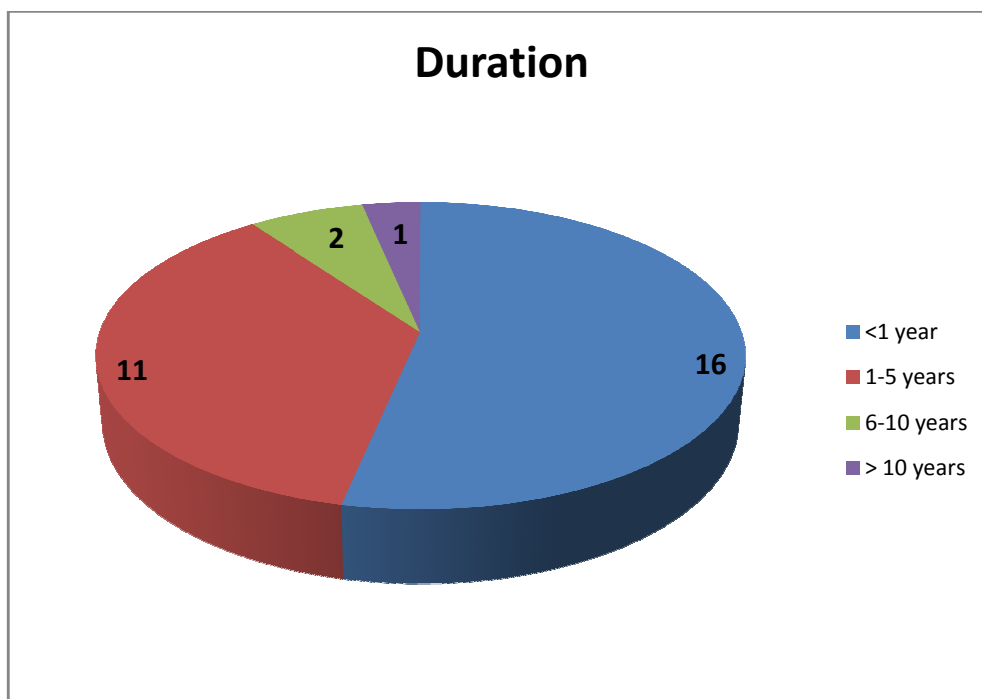


All cases of solitary nodules presented with swelling in front of neck. Association with pressure symptoms and enlarged cervical lymph nodes is rare. Toxic symptoms were present in 4 patients. In this study, 1 patient had regional lymphadenopathy; which on FNAC proved to be secondary deposits from papillary carcinoma. 4 patients had difficulty in swallowing and 6 patients, pain over the swelling. 2 patients had difficulty in breathing, which was mostly uncharacteristic; neither exertional nor positional.

**TABLE 4**  
**DURATION OF SWELLING**

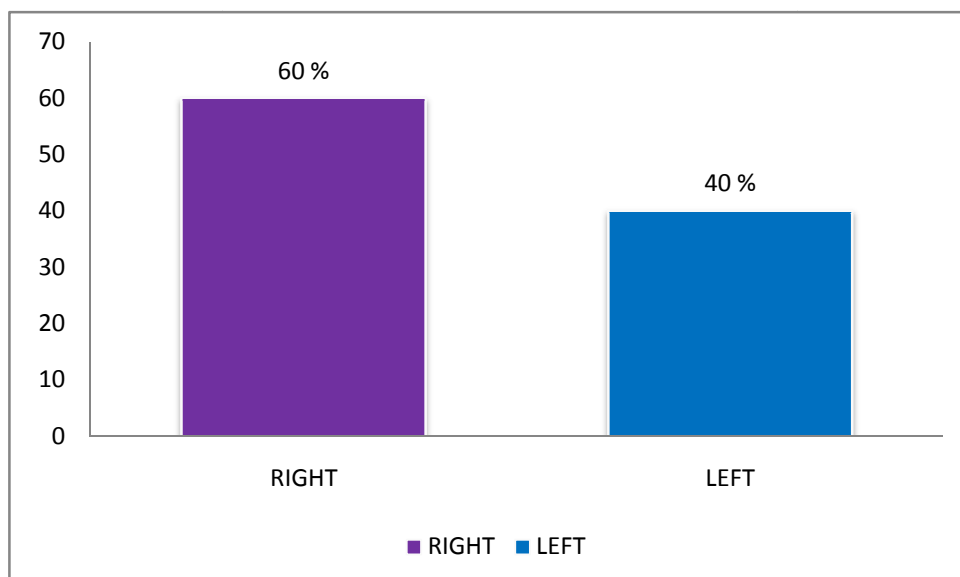
<b>DURATION</b>	<b>NO. OF PATIENTS</b>	<b>PERCENTAGE</b>
<b>&lt; 1 YEAR</b>	16	53.33%
<b>1-5 YEARS</b>	11	36.67%
<b>6 – 10 YEARS</b>	2	6.67%
<b>&gt;10 YEARS</b>	1	3.33%

There is no difference between benign and malignant nodule with regard to duration of symptoms varied from 1 month to 15 years.



**TABLE-5**  
**SIDE OF INVOLVEMENT**

<b>SIDE</b>	<b>NO. OF PATIENTS</b>	<b>PERCENTAGE</b>
<b>RIGHT</b>	18	60%
<b>LEFT</b>	12	40%



Nodules were more frequently seen in right lobe. Isthmus was not involved in any patient.

**TABLE-6**

**HORMONAL STATUS (CLINICAL)**

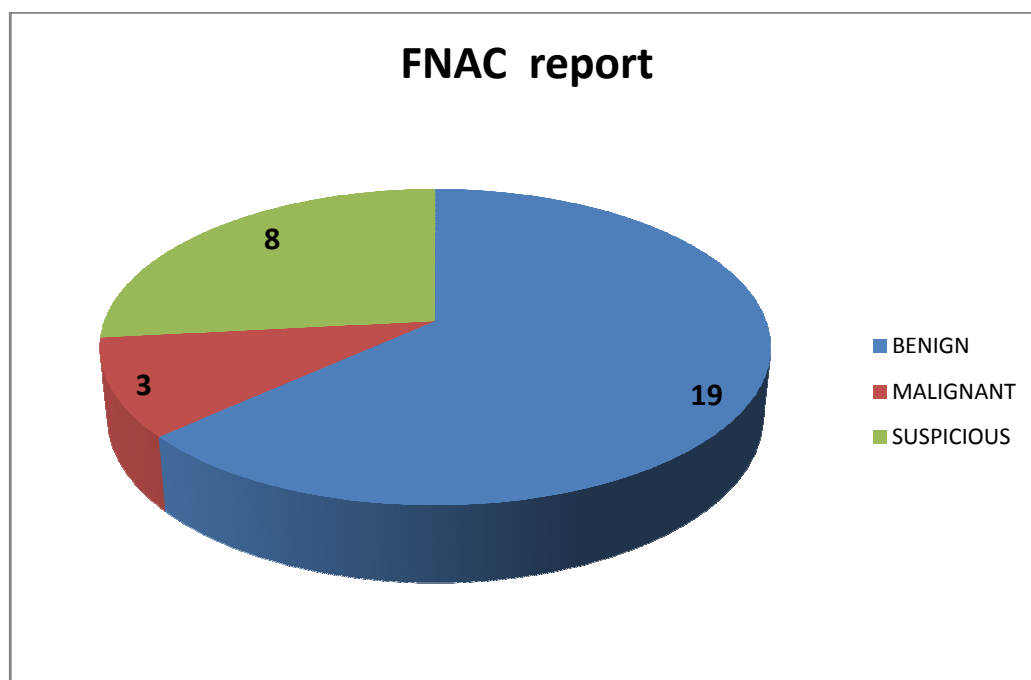
<b>HORMONAL STATUS</b>	<b>TOTAL NO. OF PATIENTS</b>	<b>PERCENTAGE</b>
<b>EUTHYROID</b>	19	63.33%
<b>HYPERTHYROID</b>	5	16.67%
<b>HYPOTHYROID</b>	6	20%

**DIAGNOSTIC WORKUP:**

In this study the following investigations were done in all patients which included urine analysis, blood sugar, urea, and serum creatinine, plain radiograph of neck, IDL scopy, chest radiograph and fine needle aspiration cytology. USG was done in all cases. Serum T3, T4 and TSH estimation were done. CT scan done in a patient with extensive neck secondaries. Radionucleotide scanning was not done for any patients due to the non-availability of the facility in our hospital. FNAC is the investigation of choice for solitary thyroid nodule. In this study FNAC was a very dependable and an easy investigation without complications.

**TABLE-7**  
**FNAC REPORT**

SL. NO	FNAC REPORT	NO. OF PATIENTS
<b>BENIGN</b>	19	63.33%
<b>MALIGNANT</b>	3	10%
<b>SUSPICIOUS</b>	8	26.67%
<b>INSUFFICIENT</b>	-	-



FNAC is report as Benign in 63% (19 patients), malignant in 10% (3 patients) and suspicious or atypical in 27% (8 patients). No FNAC was insufficient.

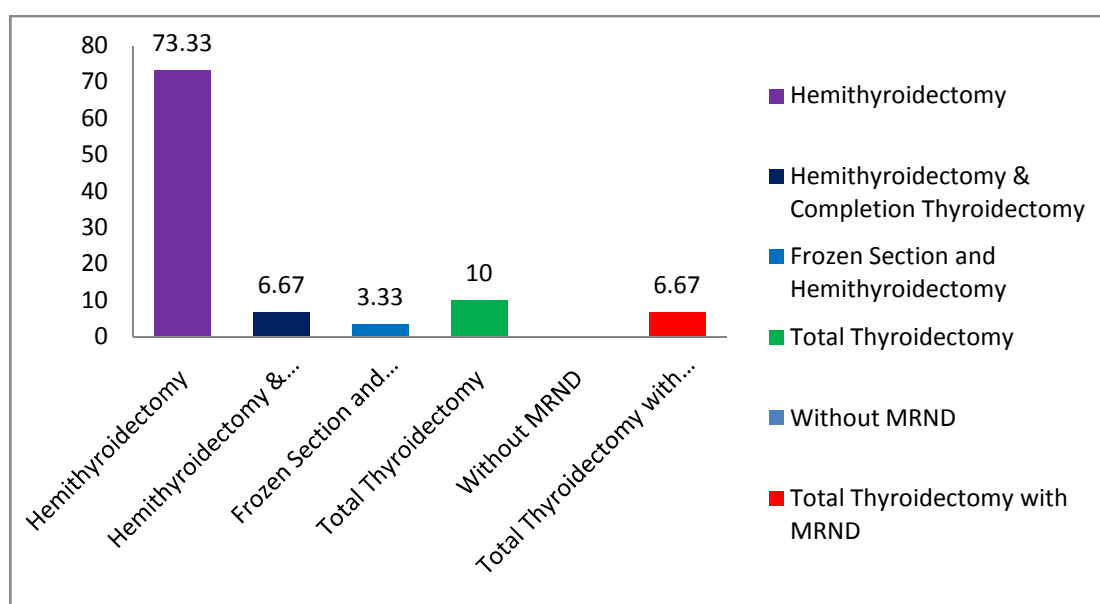
Benign reports included adenomatous and nodular colloid goiters. Malignant reports included papillary carcinoma. Suspicious reports

included follicular neoplasm, hurthle cell neoplasm, and suspicious papillary carcinomas.

Amongst the FNAC reports, nodular colloid goitre was the most common to be reported. Adenomatous goitre, presenting as a solitary nodule was next commonest eventuality. Follicular neoplasm was reported in 1 patient with the inability to indentify vascular/ capsular invasion. 3 cases were reported as papillary carcinomas with 2 of them showing deposits in neck nodes.

**TABLE-8**  
**MANAGEMENT**

MANAGEMENT	NO. OF PATIENTS	PERCENTAGE
Hemithyroidectomy	22	73.33%
Hemithyroidectomy & Completion Thyroidectomy	2	6.67%
Frozen Section and Hemithyroidectomy	1	3.33%
Total Thyroidectomy Without MRND	3	10%
Total Thyroidectomy with MRND	2	6.67%



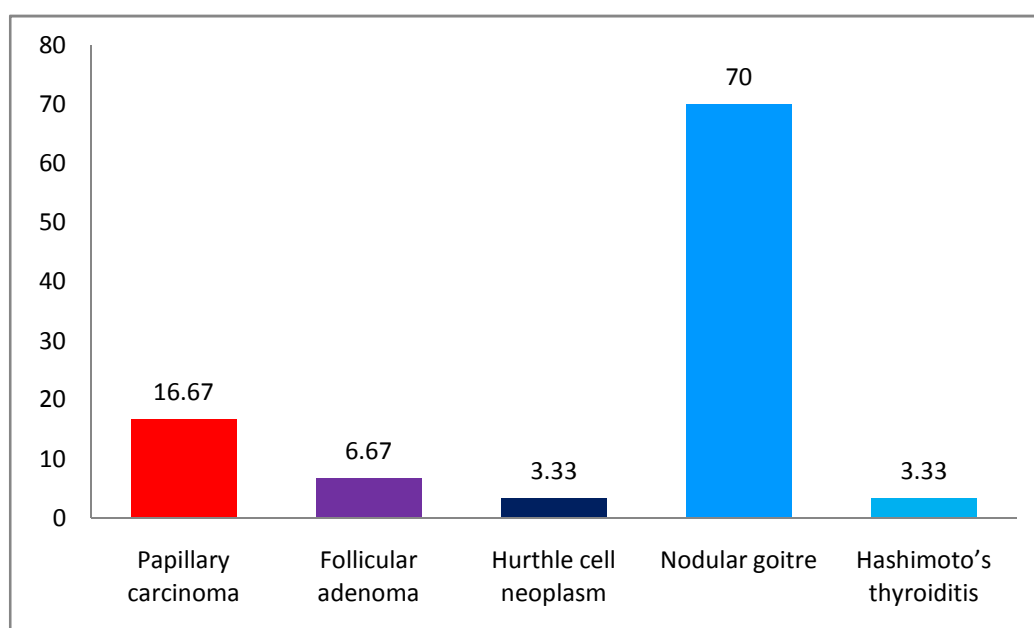
Out of 30 patients, majority of patients underwent hemithyroidectomy (22 patients, 73%). In 2 patients (7%), completion thyroidectomy was done after 4-6 weeks. Frozen section was done for 1

patient as the FNAC report was ? papillary carcinoma. But as the frozen section report was benign, she underwent only hemithyroidectomy. Total thyroidectomy was done for 2 patients of papillary carcinoma without neck nodes and 1 patient of Hurthle cell neoplasm diagnosed pre-operatively by FNAC. 2 patients who had papillary carcinoma with cervical lymph node metastasis underwent Total Thyroidectomy with modified radical neck dissection.



**TABLE-9**  
**HISTOPATHOLOGICAL REPORT**

HPE REPORT	NO. OF PATIENTS	PERCENTAGE
Papillary carcinoma	5	16.67%
Follicular adenoma	2	6.67%
Hurthle cell neoplasm	1	3.33%
Nodular goitre	21	70%
Hashimoto's thyroiditis	1	3.33%



Majority (70%) of cases were nodular goitre. Hashimoto's thyroiditis was seen in 1 patient (3%), which missed diagnosis on FNAC.

Histology proven malignancy in this series of study of solitary thyroid nodule is 16.67% of which all 5 cases were of papillary carcinoma and its variant. Of these, 3 cases were diagnosed

preoperatively and were offered the confirmative treatment. The rest two cases were diagnosed only on HPE reporting & then underwent completion total thyroidectomy without neck dissection. All these patients are under regular follow up with suppressive doses of thyroxine.

## DISCUSSION

The estimated life time risk of developing a nodule in thyroid was projected to be between 5-10%, according to a prospective study conducted in Framingham, Massachusetts, in 1950s & 1960s. According to a study conducted by Prof .R.L. Gupta University College of medical science, Delhi, right lobe involvement is more- 51.4% compared to left lobe involvement of 38.8% which is comparable with our study with the right lobe involving 60% and left lobe 40%.

In a study conducted in MKG medical college, Berhampur, Orissa (1990-1998) under Prof. M.C.Dandapat, Dr. L.M.Mukarjee concluded that the maximum number of cases were recorded during the 3rd and 4th decade of life with a female & male ratio of 5:1 which is comparable with our study which has a slightly higher ratio of 9:1. Nagori et al reported that the maximum incidence of SNT was 29% during the 4th decade.<sup>39</sup> In our study it was 30% in the 3<sup>rd</sup> decade. The commonest site of SNT was right lobe. The percentage of malignancy was 11.1% which is comparable with our study which had a percentage of 17%. In a study, Dr.H.Koticha & R.M.S Kamdar Mumbai concluded that, estimation of thyroid hormone levels has made no significant impact in deciding about surgery. FNAC is safe, simple and diagnostic but surgery is mandatory.

Usually Hyperfunctioning nodules of thyroid are thought to only rarely harbor thyroid cancer, and thus are infrequently biopsied. So in a study by Mirfakhraee et al in 2013, they present the case of a patient with

a hyperfunctioning thyroid nodule harboring carcinoma, and hence determine the prevalence of and characteristics of malignant “hot” nodules as a group. They revealed an estimated 3.1% of malignancy.<sup>1</sup>

After an analysis of 100 cases of thyroid nodules, Prof. R.C. Suryaprakash concluded that among the thyroid disorders, adenoma thyroid was the commonest among benign lesions and papillary carcinoma was the commonest malignancy. Hashimoto’s thyroiditis has got the highest incidence among the middle aged women.

### **RISK FACTORS FOR THYROID MALIGNANCY**

According to study by Yang et al in 2013, Male gender, microcalcification and cervical lymphadenopathy were independent risk factors related to malignancy in patients with solitary thyroid nodule. Patients with 2 or more risk factors should be subjected to further examination or thyroidectomy.<sup>2</sup>

### **Comparison of pre-operative FNAC with post-operative**

#### **Histopathological examination:**

Out of 30 cases operated, 4 had different HPE reports as compared to FNAC reports. If both FNAC & HPE are benign or malignant they are considered as true positive. 1 cytologically malignant lesion was reported as benign. So FNAC was false positive in this case. There were no false negative cases. Among 8 cytologically suspicious lesions, 5 cases were reported as benign and 3 cases were malignant on HPE.

**TABLE-10****ACCURACY RATE OF FNAC**

<b>RESULT</b>	<b>NO. OF PATIENTS</b>
<b>TRUE POSITIVE</b>	2
<b>TRUE NEGATIVE</b>	19
<b>FALSE NEGATIVE</b>	0
<b>FALSE POSITIVE</b>	1

$$\text{Accuracy: } \frac{TP+TN}{TP+TN+FP+FN} = \frac{2+19}{22} = \mathbf{95.45\%}$$

$$\text{Sensitivity: } \frac{TP}{TP+FN} = \frac{2}{2} = \mathbf{100\%}$$

$$\text{Specificity: } \frac{TN}{TN+FP} = \frac{19}{20} = \mathbf{95\%}$$

In comparison an overall accuracy rate greater than 95% was achieved in the cytological diagnosis of SNT. The main goal of FNAC is to accurately predict which nodule is cancerous. Sensitivity was 100% and Specificity 95%. Numerous studies cited the following data. Overall accuracy rate is estimated to be 92-95%. According to an Iranian study by I Wahad et al in 2011, the diagnostic yield of FNAC was accuracy

82.92%, sensitivity 88.09% and specificity 77.50%. <sup>40</sup> FNAC was said to have a key role in diagnosis of solitary thyroid nodules because it is safe, minimally invasive and a cost effective diagnostic tool.

#### **COMPARISON OF FNAC WITH OTHER STUDIES ENLISTED BELOW**

<b>STUDY</b>	<b>SENSITIVITY</b>	<b>SPECIFICITY</b>	<b>ACCURACY</b>
This study	100%	95%	95.45%
Indian Journal of Otorhinolaryngology, 2002 <sup>41</sup>	83.3%	100%	-
Iranian Journal of Otorhinolaryngology, 2011	88.09%	77.50%	82.92%
Gupta et al, 2010 <sup>42</sup>	80%	86.6%	73.3%

According to a study by Yeung et al in 2008, the aim of management is to identify which nodules warrant further investigation to exclude the presence of malignancy. FNAB is essential to decision making and provides highly accurate information that will ultimately determine the management of a nodule. <sup>43</sup>

**TABLE- 11**

**INCIDENCE OF MALIGNANCY IN INDETERMINATE LESIONS  
ON FNAC**

<b>TOTAL NO. OF CASES</b>	<b>NO. OF MALIGNANCIES (BIOPSY PROVED)</b>	<b>PERCENTAGE</b>
8	3	37.5%

Incidence of malignancy in indeterminate lesions is 37.5% and 62.5% of cases were benign.

**CANCER RISK IN FOLLICULAR NEOPLASM**

The cytological appearances of follicular adenoma and carcinoma are very similar. So a cytological diagnosis of follicular neoplasm is only possible, and confirmation of diagnosis of follicular carcinoma depends upon the visualization of capillary & capsular invasion in HPE. Although the cancer risk is only 20%, CFJ RUSSEL, in common with others advises surgical resection of all solitary thyroid nodules reported as follicular neoplasm cytologically. In this study 2 cases were diagnosed as follicular neoplasm cytologically and of these 4 were both were benign. Fenn & Krishnan (1976) & others found that there was no great sex predominance in the incidence of malignancy.<sup>44</sup> A solitary nodule in very young patients is almost always malignant & in middle age it is rarely

malignant and the incidence of malignancy increases with age according to Selwyn & Taylor in 1969.

**The incidence of thyroid cancer in patients with a solitary thyroid nodule as follows**

Study by Kendall & Condon 1969 } Pnarras et al 1972} <sup>45</sup>	11-20%
Study by Colin F J Russell at Royal Victoria hospital, BELFAST., UK	13%
Study by Fenn & Krishnan at CMC Vellore, Tamilnadu <sup>44</sup>	12.6%
Study by Nagori et al 1992 <sup>39</sup>	11%
Study by Dr.L.M.Mukerjee & Prof.M.C. Dandapet, MKG medical college, Berhampur Orissa	11.1%
Study conducted in PSG IMSR, Coimbatore, 2014	16.67%

This compares well with the other studies on solitary nodule goitre. The maximum incidence of malignancy of 10% of cases was present during the 5<sup>th</sup> decade.



**TABLE- 12**

**AGE AND SEX DISTRIBUTION OF BENIGN AND MALIGNANT  
NODULE**

<b>AGE IN YEARS</b>	<b>MALES</b>			<b>FEMALES</b>		
	<b>BENIGN</b>	<b>MALIGNANT</b>	<b>TOTAL</b>	<b>BENIGN</b>	<b>MALIGNANT</b>	<b>TOTAL</b>
<b>UPTO 20</b>	0	0	0	0	1	1
<b>21-30</b>	0	0	0	6	1	7
<b>31-40</b>	1	0	1	8	0	8
<b>41-50</b>	1	1	2	1	2	3
<b>51-60</b>	0	0	0	5	0	5
<b>ABOVE 60</b>	0	0	0	3	0	3
<b>TOTAL</b>	2	1	3	23	4	27

In this study, 5 patients had malignancy, out of which 4 were female patients and 1 of them male, who was in his 5<sup>th</sup> decade as comparable to a study by Lt Nagori in 1992 where the incidence in male was common in 5<sup>th</sup> and 6<sup>th</sup> decades.<sup>39</sup>

33% of solitary nodule in males proved to be malignant whereas in females only about 15% of the solitary nodules harboured malignancy.

According to Matheson 1986, the malignant potential of a nodule in a man is approximately three times that for a woman of comparable age and in our study, the risk has been two times.<sup>46</sup> Malignancy is more likely in a nodule in a child or a teenager or when goitre develops in a patient aged 60 years & above (Hamming et al 1990, Caruso and Mazzaferri 1991).<sup>47</sup>

In this study, all thyroid cancers occurred in individuals under 50 years of age and all of them were papillary carcinoma. Fravenhofer et al (1979) in his study of 125 cases of thyroid cancer, found that 80% of thyroid cancers in individuals less than 40 years of age were papillary carcinoma.<sup>48</sup>

According to a study by Khan et al in 2012, Papillary carcinoma was most common among all thyroid malignancies in patients with solitary thyroid nodules which is comparable with our study. Out of 19 malignant cases, 12( 63.16%) were papillary carcinoma, 5(26.31%) were follicular carcinoma and 2(10.53%) cases were medullary carcinoma.<sup>49</sup>

No follicular carcinoma, medullary carcinoma, anaplastic carcinoma and lymphoma were reported in our series. The relative incidence of primary malignant tumors in our series is almost in accordance with most of the reported series.

## **SURGICAL PROCEDURES FOR CARCINOMA**

We have done total thyroidectomy with or without neck dissection in five patients. Among them, 4 were papillary carcinoma and 1 was Hurthle cell adenoma. Total thyroidectomy is considered not only as a measure to reduce the recurrence rate of differentiated carcinoma but also as a means of preventing development of a highly undifferentiated lesion. The percentage of radioiodine pick up can be increased several fold after total thyroidectomy and it also increases the sensitivity of thyroglobulin as a postoperative marker of residual/recurrent disease.

2 patients underwent completion thyroidectomy after 4-6 weeks. Frozen section was done for 1 patient as the FNAC report was suspicious of papillary carcinoma. But as the frozen section report was benign, she underwent only hemithyroidectomy.

## **DISADVANTAGE**

The risk of permanent hypoparathyroidism or recurrent laryngeal nerve damage is high. Ipsilateral lobectomy with isthmusectomy is what is required in all patients with differentiated carcinoma of favourable prognosis as given in AGES scoring system (HAY ID).

The favourable prognostic factors are lesions less than 2 cm without cervical or distant metastasis, age less than 40 years in males and less than 45 years in females

So, the above patients were advised completion surgery with suppressive dose of thyroxine and regular follow-up.

The indications for isotope scanning after operation for differentiated cancer are.

1. Unresectable local recurrence
2. Metastatic disease
3. High risk patients and
4. Those with increase in serum Thyroglobulin level.

### **MALIGNANCY IN A TOXIC NODULE**

Majority of cancers arise in hypo or cold thyroid nodules (ALDERSON et al 1976<sup>50</sup> and COX et al 1991<sup>51</sup>. The possibility of malignancy occurring within a hot nodule is rare.

### **HISTOPATHOLOGICAL REPORT**

In our study, all 5 patients with malignancy were reported as papillary carcinoma. 5 patients with clinical toxicity were reported as nodular colloid goitre in HPE. 8 cases were reported as adenoma in HPE report. 70% of operated cases were diagnosed as nodular goitre. Hemithyroidectomy done for most of them.

## **OUT COME OF THERAPY**

### ***Complications:***

Out of the 30 patients operated, two developed features of hypocalcaemia in the immediate postoperative period and were revived with intravenous calcium gluconate and with no need for oral calcium supplementation.

Two patients had sluggish movement of left vocal cord after total thyroidectomy and improved later. None of the patients had postoperative wound infection. We had no mortality during this study.

So to conclude, according to a study by Frates et al in 2006, A solitary nodule had a higher likelihood of malignancy than a nonsolitary nodule. The study demonstrates that the combination of patient gender, nodule composition and presence of complications can be used to assign risk of cancer to each individual nodule.<sup>52</sup>

## CONCLUSIONS

- From our study, the common causes of SNT are nodular colloid goitre and follicular adenoma, in the benign variety while papillary carcinoma was the only malignant cause.
- Among the SNT, nodular colloid goitre (70%) is the most common lesion & papillary carcinoma (17%) is the most common malignancy.
- The incidence of SNT is very high among females (90%) compared with to males (10%), the female to male ratio being 9:1, but the malignancy rate is high among males (33%) compared to females (15%).
- SNT is more common in the right lobe (60%) than the left lobe (40%).
- The incidence of malignant lesion is 16.67%.
- The incidence of SNT is highest in the age group of 21-40 years with 53% of patients falling in this age category.
- All thyroid carcinomas were under the age of 50years and they were all papillary carcinoma.
- FNAC is the gold standard test for evaluating SNT with accuracy rate of 95.5%, sensitivity of 100% and specificity of 95%.
- The incidence of malignancy in indeterminate lesions is 37.5%.

- A selective surgical policy for Solitary Thyroid Nodule is being followed in our hospital which has been mentioned above.
- Hemi thyroidectomy is the minimum surgical procedure for solitary nodule, with completion thyroidectomy being done for all thyroid carcinomas.
- Frozen section is also gaining a significant role as it reduces the need for a second surgery.
- Patient being submitted to Thyroidectomy should be counselled preoperatively with regard to the risk of recurrent Laryngeal nerve paralysis.
- A surgical procedure in any form remains diagnostic as well as therapeutic even though the trend now is non-surgical management with close follow up for the most of the benign lesions.
- HPE remains to be the final diagnostic proof. According to these results, the management strategies varies.
- Follow up is essential in SNT because unlike other malignancies, thyroid carcinomas are easily amenable to cure, have got better prognosis & prolonged survival rate.

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## **ABBREVIATIONS**

SNT	-	SOLITARY NODULE THYROID
FNAC	-	FINE NEEDLE ASPIRATION CYTOLOGY
FA	-	FOLLICULAR ADENOMA
NG	-	NODULAR GOITRE
PC	-	PAPILLARY CARCINOMA
HT	-	HEMITHYROIDECTOMY
TT	-	TOTAL THYROIDECTOMY
CT	-	COMPLETION THYROIDECTOMY
MRND	-	MODIFIED RADICAL NECK DISSECTION
FS	-	FROZEN SECTION

## **PROFORMA**

### **PARTICULARS OF THE PATIENTS:**

- **Name**
- **Sex**
- **Age**
- **Occupation**
- **Address**

### **COMPLAINTS AND DURATION**

#### **HISTORY OF PRESENTING ILLNESS:**

- **Swelling**
- **Pain**
- **Pressure symptoms**
- **Hyper/hypothyroidism**
- **Toxic symptoms**
- **Cervical Lymphadenopathy**

#### **PERSONAL HISTORY**

#### **FAMILY HISTORY**

#### **PAST HISTORY**

#### **MENSTRUAL HISTORY**

#### **GENERAL EXAMINATION**

#### **VITAL DATA**

- **Pulse**
- **Bp**

## **LOCAL EXAMINATION**

- **Inspection**
- **Palpation**
- **Percussion**
- **Auscultation**
- **Regional lymph nodes**

## **OTHER SYSTEMS**

- **Cvs**
- **Rs**
- **Abdomen**

## **INVESTIGATIONS:**

- **Ultrasound neck**
- **FNAC**
- **Indirect laryngoscopy**

## **OPERATIVE FINDINGS**

## **BIOPSY**



S. NO	NAME	AGE	SEX	IP NO.	DURATION OF SWELLING	CLINICAL PRESENTATION							SIDE	FNAC	HPE	MANAGEMENT
						SWELLING	PAIN	DYSPOEA	DYSPHAGIA	TOXICITY	HYPOTHYROIDISM	LYMPH NODE				
1	VISALAKSHI	27	F	I14004642	10 YEARS	P							R	NG	NG	HT
2	SEERAMMAL	53	F	I14004386	2 YEARS	P							R	NG	NG	HT
3	SARASWATHY	60	F	I14004390	1 YEAR	P			P				L	NG	NG	HT
4	SANDHYA	25	F	I14004599	6 MONTHS	P							R	NG	NG	HT
5	DEVI	40	F	I14005389	6 MONTHS	P							R	HURTHLE	HURTHLE	TT
6	PRANATI	73	F	I14005835	6 MONTHS	P		P					L	FA	NG	HT
7	SAMY DASS	34	M	I14007233	1 WEEK	P	P						R	PC	FA	HT
8	LAKSHMI	38	F	I14007371	1 WEEK	P	P						R	NG	NG	HT
9	NIRMALA DEVI	32	F	I14008869	4 YEARS	P							L	PC	NG	TT
10	RAMASAMY	42	M	I14009414	2 YEARS	P					P		R	PC	PC	TT
11	WILSON MANUEL	48	M	I14009697	1 MONTH	P							R	NG	NG	HT
12	LAKSHMI	64	F	I14009961	2 MONTHS	P			P				R	NG	NG	HT
13	DORATHY	38	F	I14010446	2 YEARS	P			P				L	NG	NG	HT

14	NOORJAHAN	26	F	I14010793	2 YEARS	P				P			L	NG	NG	HT
15	SATHYA	26	F	I14011590	1 YEAR	P	P						R	NG	NG	HT
16	KOWSALYA	17	F	I14011645	6 MONTHS	P	P				P		R	FA	PC	HT+CT
17	CELIN FATHIMA	56	F	I14013182	1 YEAR	P							L	NG	NG	HT
18	SUSEELA	58	F	I14012827	1 YEAR	P							R	NG	NG	HT
19	VIMALA	39	F	I14013677	15 YEARS	P				P			L	NG	NG	HT
20	AMSAVALLI	29	F	I14014135	4 MONTHS	P							L	PC	PC	TT & LND
21	PAPPATHY	60	F	I14014966	1 MONTH	P							R	NG	NG	HT
22	YESUDIYAL	64	F	I14016230	3 MONTHS	P		P					R	NG	NG	HT
23	MYNA	44	F	I14016397	6 MONTHS	P	P				P		R	PC	PC	HT+CT
24	SAROJINI	34	F	I14017445	6 MONTHS	P			P		P		R	NG	NG	HT
25	KANNIAMMAL	45	F	I14017581	6 MONTHS	P						P	L	PC	PC	TT & LND
26	CHELLAMMAL	45	F	I14017862	2 YEARS	P					P		L	NG	NG	HT
27	MEKALA	26	F	I14021433	1 YEAR	P							L	FA	FA	HT
28	KAVITHA	39	F	I14021678	5 MONTHS	P	P				P		R	PC	HASHI	FS & HT
29	LAKSHMI	25	F	I14023175	2 MONTHS	P				P			L	NG	NG	HT
30	BINDU THOMAS	38	F	I14024268	8 YEARS	P				P			R	NG	NG	HT